# UNITED STATES
# SECURITIES AND EXCHANGE COMMISSION

**Washington, D.C. 20549**

# FORM 10-K

**(Mark One)**

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

**For the fiscal year ended: December 31, 2017**

**Or**

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

**For the transition period from to**

**Commission file number: 001-35837**

# TETRAPHASE PHARMACEUTICALS, INC.

**(Exact Name of Registrant as Specified in Its Charter)**

| **Delaware** | **04-3581650** |
|---|---|
| **(State or Other Jurisdiction of Incorporation or Organization)** | **(I.R.S. Employer Identification No.)** |

**480 Arsenal Way**
**Watertown, Massachusetts 02472**
**(Address of Principal Executive Offices) (zip code)**

**Registrant's telephone number, including area code: (617) 715-3600**
**Securities registered pursuant to Section 12(b) of the Act:**

| **Title of each class** | **Name of each exchange on which registered** |
|---|---|
| **Common Stock, $.001 par value** | **NASDAQ Global Select Market** |

**Securities registered pursuant to Section 12(g) of the Act:**
**None**

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☒

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ☐ No ☒

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes ☒ No ☐

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§229.405) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☒

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company or an emerging growth company. See definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act. (Check one):

| | | | |
|---|---|---|---|
| Large accelerated filer | ☐ | Accelerated filer | ☒ |
| Non-accelerated filer | ☐ (Do not check if a smaller reporting company) | Smaller reporting company | ☐ |
| | | Emerging growth company | ☐ |

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

The aggregate market value of the registrant's common stock, $0.001 par value per share ("Common Stock"), held by non-affiliates of the registrant, based on the last reported sale price of the Common Stock on the NASDAQ Global Select Market at the close of business on June 30, 2017, was $269,502,064. For purposes hereof, shares of Common Stock held by each executive officer and director of the registrant and entities affiliated with such executive officers and directors have been excluded from the foregoing calculation because such persons and entities may be deemed to be affiliates of the registrant. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

The number of shares outstanding of the registrant's Common Stock as of March 2, 2018: 51,629,987

**Documents incorporated by reference:**

Portions of our definitive proxy statement for our 2018 annual meeting of stockholders are incorporated by reference into Part III of this Annual Report on Form 10-K.

**TETRAPHASE PHARMACEUTICALS, INC.**
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**References to Tetraphase**

Throughout this Annual Report on Form 10-K, the "Company," "Tetraphase," "we," "us," and "our," except where the context requires otherwise, refer to Tetraphase Pharmaceuticals, Inc. and its consolidated subsidiaries, and "our board of directors" refers to the board of directors of Tetraphase Pharmaceuticals, Inc.

The trademarks, trade names and service marks appearing in this Annual Report on Form 10-K are the property of their respective owners.

**Forward-Looking Information**

This Annual Report on Form 10-K contains forward-looking statements regarding, among other things, our future discovery and development efforts, our future operating results and financial position, our business strategy, and other objectives for our operations. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "would" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. You also can identify them by the fact that they do not relate strictly to historical or current facts. There are a number of important risks and uncertainties that could cause our actual results to differ materially from those indicated by forward-looking statements. These risks and uncertainties include those inherent in pharmaceutical research and development, such as adverse results in our drug discovery and clinical development activities, decisions made by the U.S. Food and Drug Administration and other regulatory authorities with respect to the development and commercialization of our drug candidates, our ability to obtain, maintain and enforce intellectual property rights for our drug candidates, our ability to obtain any necessary financing to conduct our planned activities, and other risk factors. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this Annual Report on Form 10-K, particularly in the section entitled "Risk Factors" in Part I that could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments that we may make. Unless required by law, we do not undertake any obligation to publicly update any forward-looking statements.

## PART I

### ITEM 1. Business

**Overview**

We are a clinical-stage biopharmaceutical company using our proprietary chemistry technology to create novel antibiotics for serious and life-threatening multidrug-resistant infections. We are developing our lead product candidate, eravacycline, a fully synthetic fluorocycline, as an intravenous, or IV antibiotic for use as a first-line empiric monotherapy for the treatment of multidrug-resistant infections, including multidrug-resistant, or MDR, Gram-negative infections, such as those found in complicated intra-abdominal infections, or cIAI.

We conducted a global phase 3 clinical program for eravacycline called IGNITE (**I**nvestigating **G**ram-**N**egative **I**nfections **T**reated with **E**ravacycline).

On July 25, 2017, we announced top-line data from our IGNITE4 trial, a global phase 3 randomized, double-blind, double-dummy, multicenter, prospective study assessing the efficacy, safety and pharmacokinetics of twice-daily intravenous, or IV, eravacycline (1.0 mg/kg every 12 hours) compared with meropenem (1g every 8 hours) for the treatment of cIAI that we conducted in 500 patients. In the trial, eravacycline met the primary endpoint of statistical non-inferiority of clinical response at the test-of-cure, or TOC, visit, under the guidance set by the United States Food and Drug Administration, or FDA, and the European Medicines Agency, or EMA. Prior to IGNITE4, we conducted IGNITE1, a phase 3 clinical trial of twice daily IV eravacycline (1.0 mg/kg every 12 hours) compared with ertapenem (1.0g IV every 24 hours) for the treatment of cIAI. In IGNITE1, eravacycline met the primary endpoint of statistical non-inferiority of clinical response.

On January 2, 2018, we announced the submission of a new drug application, or NDA, to the FDA for IV eravacycline for the treatment of cIAI. The NDA submission includes data from the IGNITE1 and IGNITE4 phase 3 clinical trials. In February 2018, the FDA notified us that it had completed its initial 60-day review of our NDA and August 28, 2018 was set as our Prescription Drug User Fee Act, or PDUFA, goal date for the FDA's completion of its review of our NDA. In the third quarter of 2017 we submitted a marketing authorization application, or MAA, to the EMA for IV eravacycline for the treatment of cIAI primarily based upon the results of IGNITE1.

The FDA has granted Qualified Infectious Disease Product (QIDP) and Fast Track designations for IV eravacycline for cIAI.

In February 2018, we announced top-line data from our IGNITE3 trial, a global phase 3 randomized, multi-center, double-blind, clinical trial evaluating the efficacy and safety of once-daily intravenous, or IV, eravacycline, at a dose of 1.5mg/kg every 24 hours, compared to ertapenem, at a dose of 1g every 24 hours, for the treatment of complicated urinary tract infections, or cUTI, that we conducted in 1,205 patients who were randomized 1:1 to receive eravacycline or ertapenem for a minimum of 5 days, and then were eligible for transition to an appropriate approved oral agent. In this trial, eravacycline did not meet the co-primary endpoints of responder rate, a combination of clinical cure and microbiological success, in the microbiological intent-to-treat, or micro-ITT, population at the end-of-IV treatment visit and at the test-of-cure visit (5-10 days post therapy). Given the IGNITE3 results, we are no longer evaluating IV eravacycline for the treatment of cUTI and have also ceased development of an oral formulation for eravacycline for the treatment of cUTI.

Eravacycline is designed to treat a broad range of infections, including infections due to multidrug-resistant bacteria. In *in vitro* experiments, eravacycline has demonstrated the ability to cover a wide variety of multidrug-resistant Gram-negative, Gram-positive, anaerobic and atypical bacteria, including multidrug-resistant *Klebsiella pneumoniae* and multi-drug resistant *Acinetobacter.* Multidrug-resistant *Klebsiella pneumoniae* is one of the carbapenem-resistant *Enterobacteriaceae* (or CREs) listed as an urgent threat and multi-drug resistant *Acinetobacter* is listed as a serious threat by the Centers for Disease Control and Prevention, or CDC, in a September 2013 report and they are listed as Priority 1; Critical pathogens in the World Health Organization's priority pathogens list for R&D, published in February 2017. CREs were a confirmed area of great concern by the World Health Organization in an April 2014 global surveillance report. Gram-negative bacteria that are resistant to multiple available antibiotics are increasingly common and a growing threat to public health. We believe that the ability of eravacycline to cover multidrug-resistant Gram-negative bacteria, as well as multidrug-resistant Gram-positive, anaerobic and atypical bacteria, will enable eravacycline to become the drug of choice for first-line empiric treatment of patients with cIAI.

In 2011 and 2012, the U.S. government awarded contracts for potential funding of over $100 million for the development of our antibiotic compounds, which today consist of eravacycline, TP-6076 and TP-271. These awards include a contract for up to $67.3 million from the Biomedical Advanced Research and Development Authority, or BARDA, an agency of the U.S. Department of Health and Human Services, for the development of eravacycline for the treatment of disease caused by bacterial biothreat pathogens. We refer to this contract as the BARDA Contract. The funding under the BARDA Contract was used for certain activities in the development of eravacycline to treat cIAI and, prior to the IGNITE3 results, cUTI. These awards also include a contract for up to $35.8 million from the National Institute of Allergy and Infectious Diseases, or NIAID, a division of the National Institutes of Health, for the development of TP-271. We refer to this contract as the NIAID Contract. In addition, during 2011, NIAID awarded a separate grant for $2.9 million. We refer to this award as the NIAID Grant. These awards were made to CUBRC, Inc., or CUBRC, an independent, not-for-profit, research corporation that specializes in U.S. government-based contracts, with which we are collaborating. CUBRC serves as the prime contractor under these awards, primarily carrying out a program management and administrative role with additional responsibility for the management of preclinical studies. We serve as lead technical expert on all aspects of these awards and also serve as a subcontractor of CUBRC responsible for management of chemistry, manufacturing and control activities and clinical studies. The BARDA Contract includes funding for some of the activities that we would otherwise have been required to fund on our own in connection with our NDA submission for eravacycline.

In March 2017, the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator, or CARB-X, an international public-private partnership focused on advancing new antimicrobial products to address the threat of antibiotic resistance, selected us to receive up to $4.0 million in research funding over 18 months for TP-6076. In connection with this funding, we entered into a cost reimbursement Sub-Award Agreement with the Trustees of Boston University, the administrator of the program. We began recognizing revenue from the Sub-Award Agreement in April 2017. Although the Sub-Award Agreement has a term which currently expires on December 31, 2018, the project can be terminated for convenience at any time.

**Strategy**

Our goal is to become a fully integrated biopharmaceutical company that discovers, develops and commercializes novel antibiotics, such as eravacycline, for use in areas of unmet medical need. Key elements of our strategy include:

- ***Seek regulatory approval for IV eravacycline for the treatment of cIAI***. We have completed two phase 3 clinical trials of IV eravacycline in patients with cIAI – IGNITE1 and IGNITE4. We submitted an NDA to the FDA for IV eravacycline for the treatment of cIAI based on the results of IGNITE1 and IGNITE4. We have also submitted an MAA to the EMA for IV eravacycline for the treatment of cIAI based on the results of IGNITE1. Both the NDA and the MAA are currently under review by the respective regulatory agencies. The PDUFA goal date is August 28, 2018 for the FDA to complete its review of our NDA.
- ***Maximize the commercial potential of eravacycline for the treatment of cIAI***. If eravacycline is approved for the treatment of cIAI, we intend to directly commercialize eravacycline in the United States with a targeted hospital sales force and to commercialize eravacycline in other regions through collaboration arrangements, such as the collaboration agreement we entered into with Everest Medicines Limited in February 2018. We believe that eravacycline's potent coverage of multidrug-resistant Gram-negative bacteria and other multidrug-resistant bacteria, will allow it to be used to treat cIAI patients successfully in hospitals, Skilled Nursing Facilities (SNF), and Long Term Acute Care Hospitals (LTACH).
- ***Pursue development of eravacycline in additional indications***. We are developing eravacycline for the treatment of cIAI, and, subject to obtaining additional financing, intend to pursue development of eravacycline for the treatment of additional indications, including other serious and life-threatening infections. We may pursue these development activities either by ourselves or with collaborators
- ***Opportunistically advance development of other product candidates created using our proprietary chemistry technology***. In addition to eravacycline, we are currently conducting phase 1 clinical trials of TP-271 and TP-6076. We intend to advance our antibiotic product pipeline with differentiated product candidates created using our proprietary chemistry technology and targeting hospital and acute care markets. We may pursue these activities either by ourselves or with collaborators.

**Drug-Resistant Antibiotic Market**

Physicians commonly prescribe antibiotics to treat patients with acute and chronic infectious diseases that are either presumed or known to be caused by bacteria. Inappropriate use of antibiotics and lack of new therapies has resulted in a rapid increase in bacterial infections that are resistant to multiple antibacterial agents. Global microbial resistance, including bacteria, viruses and fungi, now results in the death of at least 700,000 people each year, according to an analysis commissioned by the U.K. government in 2016. The report predicts that failing to develop effective treatments for drug-resistant bacteria by 2050 would lead to 10 million extra

deaths a year. In a September 2013 report, the CDC estimated that every year in the United States, more than two million people acquire serious infections that are resistant to one or more of the antibiotics designed to treat those infections, with at least 23,000 dying as a result, and many more dying from other conditions that are complicated by the occurrence of an antibiotic-resistant infection. These antibiotic-resistant infections add considerable and avoidable costs to the U.S. healthcare system. In the same September 2013 report, the CDC noted that the total economic cost of antibiotic infections to the U.S. economy has been estimated to be as high as $20 billion in excess of direct healthcare costs. Over the last decade there has been an increase in antibiotics that target resistant Gram-positive bacteria, but there still remain limited therapeutic options for resistant Gram-negative infections. According to the CDC, among all of the bacterial resistance problems, Gram-negative pathogens are particularly worrisome because they are becoming resistant to nearly all drugs that would be considered for treatment, with the most serious Gram-negative infections being healthcare associated and the most common pathogens being *Enterobacteriaceae*, *Pseudomonas aeruginosa* and *Acinetobacter*.

Antibiotics that treat bacterial infections can be classified as broad-spectrum or narrow-spectrum. Antibiotics that are active against a mixture of Gram-positive, Gram-negative and anaerobic bacteria are referred to as broad-spectrum. Antibiotics that are active only against a select subset of bacteria are referred to as narrow-spectrum. Because it usually takes from 24 to 72 hours from the time a specimen is received in the laboratory to definitively diagnose a particular bacterial infection, physicians may be required to prescribe antibiotics for serious infections without having identified the bacteria. As such, effective first-line treatment of serious infections requires the use of broad-spectrum antibiotics with activity against a broad range of bacteria at least until the bacterial infection can be diagnosed.

Broad-spectrum antibiotics are used to treat major hospital infections such as cIAI, hospital-acquired pneumonia, or HAP, and ventilator-associated pneumonia, or VAP. Based on an analysis from a variety of industry sources, we estimate that the number of patients treated with antibiotics in the United States and European Union annually includes approximately 4.6 million cIAI patients with each patient being treated for an average of 8.6 days for a combined estimated 40 million annual average days of treatment; and 2.8 million HAP/VAP patients with each patient being treated for an average of 9.6 days for a combined estimated 27 million annual average days of treatment. Of these patients, we believe that approximately 40% of cIAI patients require a change in therapy and 50% of patients with cIAI are receiving combination therapy.

As such, at present, there is an acute need for new drugs to treat multidrug-resistant Gram-negative bacteria. Currently approved products, such as meropenem are becoming increasingly ineffective against Gram-negative bacteria due to increasing resistance, limiting patients' treatment options, particularly for patients with multidrug-resistant infections. Few new therapeutic agents have been approved or are in clinical development.

A survey of infectious disease specialists published in the June 2012 edition of *Clinical Infectious Disease* rated multidrug-resistant Gram-negative infections as the most important unmet clinical need in current practice. In the survey, 63% of physicians reported treating a patient in the past year whose bacterial infection was resistant to all available antibacterial agents. A nationwide electronic database looked at the prevalence of gram negative resistance from 2008-2015 in US Hospitals and it showed MDR rates continue to increase. Out of the 3,158,349 isolates tested 5.3% were considered MDR pathogens. Five bacteria accounted for 92.7% of all MDR isolates: *E coli* (39.4%), *P aeruginosa* (29.4%), *K pneumoniae* (13.2%), *A baumannii* (5.4%) and *Enterobacter* spp (5.2%). The highest rate of MDR was associated with the hospital onset setting (11.4%), followed by the admission period (6.6%), and the ambulatory setting (3.5%). The database showed that 42.9% of *A baumannii* were MDR related isolates. The rate of MDR *A baumannii was* highest in the inpatient setting (58.6% of isolates from all body sources), followed by admission setting (43.2%), and ambulatory setting (24.8%).

The important need for new treatment options for serious bacterial infections was further highlighted by the passage in the United States in July 2012 of the Generating Antibiotic Incentives Now, or GAIN, Act, which provides regulatory incentives for the development of new antibacterial or antifungal drugs intended to treat serious or life-threatening infections that are resistant to existing treatment. In September 2014, the United States' President's Council of Advisors on Science and Technology issued a report providing recommendations to combat the rise in antibiotic resistant bacteria and advising that without rapid action, the United States risks losing the tremendous progress made in antibiotic development over the last century. Their recommendations focused on three areas: improving surveillance, increasing longevity of current antibiotics and increasing the rate at which new antibiotics are discovered and developed.

New legislative initiatives have been approved as part of the 21st Century Cures Act, including the Antibiotic Development to Advance Patient Treatment Act which would provide a pathway for approval of antibiotics in limited populations of patients with few or no suitable treatment options. Other legislation still pending include the Developing an Innovative Strategy for Antimicrobial Resistant Microorganisms, or DISARM, Act which would designate certain novel antibiotics used to treat serious bacterial infections to receive higher Medicare reimbursement, and an amendment to the GAIN Act, which would allow successful QIDP sponsors to transfer up to one year of exclusivity to another product, including products marketed by other companies.

**Limitations of Available Treatment Options**

When confronted with a new patient suffering from a serious infection caused by an unknown pathogen, a physician may be required to quickly initiate first-line empiric antibiotic treatment to stabilize the patient prior to definitively diagnosing the particular bacterial infection. However, current antibiotics for first-line empiric treatment of serious bacterial infections suffer from significant limitations, including one or more of the following:

***Insufficient Coverage of Multidrug-resistant Bacteria.*** A physician cannot risk prescribing an inappropriate antibiotic when initially treating a patient for a serious infection where the pathogen has not yet been definitively identified. Frequently used products, such as linezoid and daptomycin, are limited to Gram-positive bacteria and thus are rarely used as a first-line empiric monotherapy if broad bacterial coverage is required. Recently approved products are limited to specific Gram-negative bacteria and thus are rarely used as a first-line empiric monotherapy if broad bacterial coverage is required. In addition, other popular antibiotics that have been used as first-line empiric monotherapies, such as levofloxacin, piperacillin/tazobactam, carbapenems, and imipenem/cilastatin, have seen their utility as first-line empiric monotherapies diminished as the number of bacterial strains resistant to these therapies has increased.

***Complicated and Expensive Multi-Drug Cocktails and Multi-Dose Regimens.*** Due to gaps in the spectrum of coverage of antibiotics, physicians are often confronted with the need to design complicated multi-drug cocktails for the first-line empiric treatment of patients with serious infections. The clinical situation is further complicated when each drug in the multi-drug cocktail has a different dosing regimen, such as three or four times a day, resulting in an added burden on the pharmacy and nursing staff, higher costs due to multiple drug administrations and an increased potential for medical errors or drug-drug interactions. We believe that, with the exception of eravacycline, most of the antibiotics that are in development or have recently been approved by the FDA that are intended to cover a broad range of bacteria, including Gram-negative bacteria, or solely to address Gram-negative bacteria, are being developed or are approved for use in combination with one or more other antibiotics, and require the addition of a third drug such as metronidazole to address the presence of anaerobic bacteria.

***Safety and Tolerability Concerns.*** Concerns about antibiotic safety and tolerability are among the leading reasons why patients stop treatment and fail therapy. Antibiotics on the market have been associated with adverse effects such as myelosuppression, seizures, nephrotoxicity and gastrointestinal disorders.

Given these limitations, there is an unmet medical need for a first-line empiric antibiotic treatment that has the following characteristics:

- Potency and effectiveness against a broad range of bacteria, including multidrug-resistant Gram-negative, Gram-positive, atypical and anaerobic bacteria;
- Capability of being used as a monotherapy in the majority of patients in the hospital with cIAI and other multidrug-resistant infections;
- A convenient dosing regimen, such as once or twice-daily; and
- A favorable safety and tolerability profile.

Based on our belief that eravacycline and our other pipeline candidates have, or potentially have, each of these characteristics, our goal is to develop eravacycline and our other pipeline candidates to be the drug of choice for first-line empiric treatment of a wide variety of serious and life-threatening infections.

**Drug Development Programs**

The following table sets forth our clinical and earlier-stage antibiotic compounds that we are developing for the treatment of serious and life-threatening infections and their status.

| Candidate | Indication | Status |
|---|---|---|
| *Eravacycline* | cIAI (IV) | Phase 3 IGNITE1 study completed; met primary end point<br>Phase 3 IGNITE4 study completed; met primary end point |
| TP-271 | Bacterial biothreats | Phase 1 clinical trials ongoing |
| TP-6076 | Multidrug-resistant Gram-negative infections | Phase 1 clinical trials ongoing |

**Eravacycline**

***Overview***

We are developing our lead product candidate, eravacycline, as an IV antibiotic for use as a first-line empiric monotherapy for the treatment of resistant and multidrug-resistant infections, including multidrug-resistant Gram-negative bacteria in patients, such as those with cIAI. We developed eravacycline using our proprietary chemistry technology.

To date, we have completed four phase 3 clinical trials with eravacycline: IGNITE1 and IGNITE4, each a phase 3 clinical trial evaluating the safety and efficacy of eravacycline with IV administration for the treatment of cIAI; IGNITE2, a phase 3 clinical trial evaluating the safety and efficacy of eravacycline with IV-to-oral transition therapy for the treatment of cUTI and IGNITE3, a phase 3 clinical trial evaluating the safety and efficacy of eravacycline with IV administration for the treatment of cUTI.

In December 2014, we announced that in IGNITE1, eravacycline met the primary endpoint of statistical non-inferiority compared to the control therapy for the trial. In the third quarter of 2017 we submitted a marketing authorization application, or MAA, to the EMA for IV eravacycline for the treatment of cIAI primarily based upon the results of IGNITE1. In July 2017, we announced that in IGNITE4, eravacycline met the primary endpoint of statistical non-inferiority compared to the control therapy for the trial. On January 2, 2018, we announced the submission of an NDA, to the FDA for IV eravacycline for the treatment of cIAI. The NDA submission includes data from the IGNITE1 and IGNITE4 phase 3 clinical trials. The PDUFA goal date is August 28, 2018 for the FDA to complete its review of our NDA.

In September 2015, we announced that eravacycline did not meet the primary endpoint of statistical non-inferiority in IGNITE2 compared to the control therapy for this trial. In February 2018, we announced that eravacycline did not meet the co-primary endpoints of statistical non-inferiority in IGNITE3 compared to the control therapy for this trial. Given the IGNITE3 results, we are no longer evaluating IV eravacycline for the treatment of cUTI and have also ceased development of an oral formulation for eravacycline for the treatment of cUTI.

Tetracycline antibiotics have been in clinical use for over 50 years and have a demonstrated record of safety and effectiveness. However, as with most classes of antibiotics, a high incidence of resistance among many bacteria has limited their effectiveness and resulted in tetracyclines being relegated to second- or third-line therapy several decades after their introduction. Chemists have generally been unable to synthesize new tetracyclines that could overcome bacterial resistance mechanisms. We have used our proprietary chemistry technology to create more than 3,000 new tetracycline derivatives that we believe could not be practically created with conventional methods. Many of these new derivatives, including eravacycline, have been able to overcome bacterial resistance in in vitro studies.

Eravacycline is a novel, fully synthetic fluorocycline antibiotic. We selected eravacycline for development from tetracycline derivatives that we generated using our proprietary chemistry technology.

In designing eravacycline, we inserted a fluorine atom into the tetracycline scaffold, which we call a fluorocycline, and modified the scaffold at another position. We believe that these modifications enable eravacycline to not be subject to tetracycline-specific mechanisms of drug resistance. As a result, we believe that eravacycline is active against multidrug-resistant bacteria in ways that tetracyclines currently on the market or in development are not.

In *in vitro* studies, including a surveillance study published in December 2014 using over 4,000 patient bacterial isolates collected in New York City, eravacycline has been highly active against emerging multidrug-resistant pathogens like *Acinetobacter baumannii* as well as clinically important species of *Enterobacteriaceae,* including those isolates that produce ESBLs or are resistant to the carbapenem class of antibiotics, and anaerobes, in comparison to commonly used antibiotics.

Data published in August 2016 demonstrated that eravacycline retained potency against *E. coli* clinical isolates containing a plasmid expressing *mcr-1* (ERV $MIC_{90}$=0.5 μg/mL; colistin $MIC_{90}$=16 μg/mL). The *in vitro* potency of eravacycline was unaffected by inducible overexpression of the *mcr-1* gene in an engineered laboratory *E. coli* strain.

Eravacycline has also demonstrated strong activity *in vitro* against Gram-positive pathogens, including both nosocomial and community-acquired methicillin susceptible or resistant *Staphylococcus aureus* strains, vancomycin susceptible or resistant *Enterococcus faecium* and *Enterococcus faecalis,* and penicillin-susceptible or resistant strains of *Streptococcus pneumoniae*. In *in vitro* studies of pathogens most prevalent in cIAI infections, eravacycline consistently exhibited strong activity against *enterococci* and *streptococci.* One of the most frequently isolated anaerobic pathogens in cIAI, either as the sole pathogen or often in conjunction with another Gram-negative bacterium, is *Bacteroides fragilis.* In these studies eravacycline demonstrated activity against *Bacteroides fragilis* and a wide range of Gram-positive and Gram-negative anaerobes.

***Key Differentiating Attributes of Eravacycline***

We believe that the following key attributes of eravacycline, observed in clinical trials and preclinical studies, differentiate eravacycline from other antibiotics targeting multidrug-resistant infections, including multidrug-resistant Gram-negative infections. We believe these attributes will make eravacycline a safe and effective treatment for cIAI and potentially other serious and life-threatening infections for which we may develop eravacycline.

- **Offers a broad range of activity against a wide variety of multidrug-resistant Gram-negative, Gram-positive and anaerobic bacteria.** In our phase 2 and phase 3 clinical trials of the IV formulation of eravacycline, eravacycline demonstrated a high cure rate against a wide variety of multidrug-resistant Gram-negative, Gram-positive and anaerobic bacteria. In addition, in *in vitro* studies, eravacycline demonstrated potent antibacterial activity against Gram-negative bacteria, including ESBL-producing *enterobacteriaceae; Carbapenemase-producing Enterobacteriaceae (CRE); MCR-1 gene resistance bacteria; Acinetobacter baumannii, including carbapenem resistant Acinetobacter (CRAB);* Gram-positive bacteria, including MRSA and vancomycin-resistant *enterococcus*, or VRE; and anaerobic pathogens. As a result, we believe that eravacycline has the potential to be used as a first-line empiric monotherapy for the treatment of cIAI and potentially other serious and life-threatening infections.
- **Lower probability of drug resistance.** To date, in the clinical trials and preclinical studies of eravacycline that we have conducted for the treatment of cIAI, we have seen little decrease in susceptibility that would suggest increased resistance to eravacycline. We believe that, as a fluorocycline, eravacycline will not be subject to tetracycline-specific mechanisms of drug resistance in certain multidrug-resistant, or MDR, pathogens.
- **Favorable safety and tolerability profile.** Eravacycline has been evaluated in over 2,700 subjects in the phase 1, phase 2 and phase 3 clinical trials that we have conducted through February 2018. In these trials, eravacycline has demonstrated a favorable safety and tolerability profile. In our phase 2 and phase 3 clinical trials of eravacycline in patients with cIAI, no patients suffered any drug-related serious adverse events, and safety and tolerability were comparable to the respective control therapies for the trials. In the phase 3 clinical trials of eravacycline in patients with cUTI, safety and tolerability were comparable to the respective control therapies for these trials. In addition, in these phase 2 and phase 3 clinical trials, the rate at which gastrointestinal adverse events such as nausea and emesis occurred in the eravacycline arms was low.
- **Convenient dosing regimen.** In our clinical trials to date, we have dosed eravacycline once or twice a day as a monotherapy. We believe that eravacycline will be able to be administered as a first-line empiric monotherapy with twice-daily dosing, avoiding the need for complicated dosing regimens typical of multi-drug cocktails and the increased risk of negative drug-drug interactions inherent to multi-drug cocktails.

***Clinical Experience***

We have studied IV and oral formulations of eravacycline in over 2,700 subjects in 21 clinical trials completed from October 2009 to February 2018.

***Phase 3 Clinical Program***

We designed our IGNITE phase 3 program for eravacycline to enable us to position eravacycline as a first-line empiric monotherapy for the treatment of cIAI and cUTI due to eravacycline's broad-range of coverage against resistant and multidrug-resistant infections, including multidrug-resistant Gram-negative infections. We are now focusing our efforts on the development of eravacycline for the treatment of cIAI.

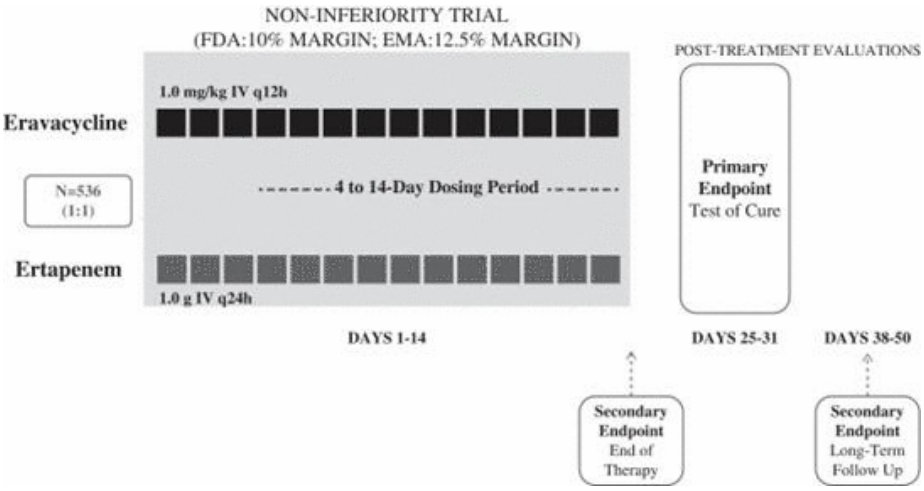
*cIAI*

Our initial phase 3 clinical trial of eravacycline for the treatment of patients with cIAI was our IGNITE1 trial. In December 2014, we announced that eravacycline met the primary endpoint of statistical non-inferiority compared to ertapenem in IGNITE1 for the treatment of cIAI. In July 2017, we announced that eravacycline met the primary endpoint of statistical non-inferiority compared to meropenem in IGNITE4 for the treatment of cIAI.

On January 2, 2018, we announced the submission of an NDA to the FDA for IV eravacycline for the treatment of cIAI. The NDA submission includes data from the IGNITE1 and IGNITE4 phase 3 clinical trials. The PDUFA goal date is August 28, 2018 for the FDA to complete its review of our NDA. In the third quarter of 2017 we submitted an MAA to the EMA for IV eravacycline for the treatment of cIAI primarily based upon the results of IGNITE1.

*IGNITE1*

**Eravacycline Phase 3 IGNITE1 Study Design**

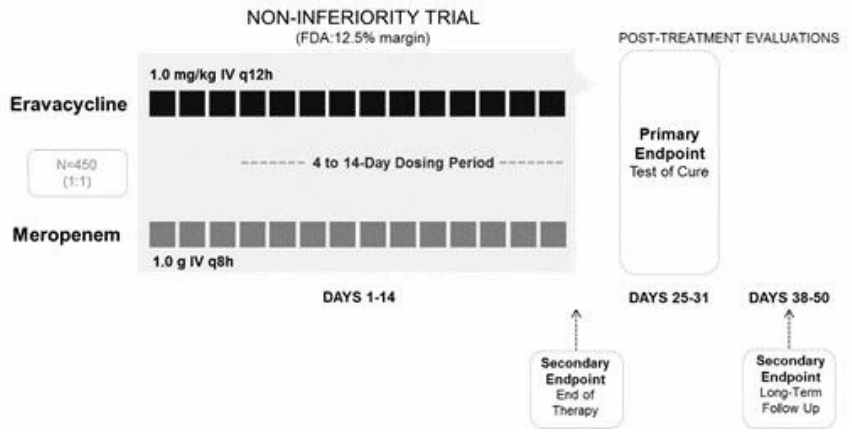



We designed IGNITE1 as a non-inferiority study. Under FDA guidance, the primary endpoint of the trial was clinical response at the TOC visit in the microbiological intent-to-treat, or micro-ITT, population which consisted of all randomized patients in the trial who had baseline bacterial pathogens that cause cIAI and against which eravacycline has antibacterial activity. Under EMA guidance, the primary endpoint of the trial was clinical response at the TOC visit in the modified intent-to-treat, or MITT, population which consisted of all patients who received at least one dose of study drug, and in the clinically evaluable, or CE, patient population, which consisted of all randomized patients in the trial who meet key inclusion/exclusion criteria and follow other important components of the trial. We designed the trial to be consistent with the FDA's cIAI guidance, in which the FDA suggested that the primary efficacy endpoint for a trial of cIAI should be complete resolution of baseline signs and symptoms attributable to cIAI in the micro-ITT patient population 28 days after randomization and the absence of clinical failure including death and unplanned surgical procedures through the period ending 28 days following randomization.

In December 2014, we announced top-line data from IGNITE1. In the trial, eravacycline met the primary endpoint of statistical non-inferiority of clinical response at the TOC visit, under the guidance set by the FDA and the EMA. The primary analysis under the FDA guidance was conducted using a 10% non-inferiority margin in the micro-ITT population. In the micro-ITT population, the lower and upper bounds of the 95% confidence interval were -7.1% and 5.5%, respectively. Under the EMA guidance, the primary analysis was conducted using a 12.5% non-inferiority margin in the CE and MITT patient populations. In the CE population, the lower and upper bounds of the 95% confidence interval were -6.3% and 2.8%, respectively, and the lower and upper bounds of the 99% confidence interval were -7.9% and 4.4%, respectively. In the MITT population, the lower and upper bounds of the 95% confidence interval were -7.4% and 3.8%, respectively, and the lower and upper bounds of the 99% confidence interval were -9.2% and 5.6%, respectively. The most commonly reported drug-related adverse events for eravacycline were gastrointestinal, including nausea (3.3%) and emesis (2.2%). This adverse event profile for eravacycline was consistent with that seen in the phase 2 clinical trial of eravacycline in cIAI. The spectrum of pathogens in this trial was similar to that seen in other pivotal trials of antibiotics in this patient population. The most common Gram-negative pathogens in the trial included *Escherichia coli, Klebsiella pneumonia, Pseudomonas* and *Bacteroides.*

*IGNITE4*

**Eravacycline Phase 3 IGNITE4 Study Design**




We designed IGNITE4 as a non-inferiority study. Under FDA guidance, the primary endpoint of the trial was clinical response at the TOC visit in the microbiological intent-to-treat, or micro-ITT, population, which consisted of randomized patients in the trial who had baseline bacterial pathogens that cause cIAI and against which eravacycline has antibacterial activity. Under EMA guidance, the primary endpoint of the trial was clinical response at the TOC visit in the modified intent-to-treat, or MITT, population, which consisted of patients in the trial who received at least one dose of study drug, and in the clinically evaluable, or CE, patient population, which consisted of patients in the trial who met key inclusion/exclusion criteria and followed other important components of the trial. Secondary endpoints included clinical response at the end-of-treatment, TOC and follow-up visits in the intent-to-treat population, the CE population, the micro-ITT population and the microbiologically evaluable, or ME, population. The ME population consisted of all micro-ITT patients who met key inclusion/exclusion criteria and followed other important components of the trial. In the trial, we also studied microbiologic response at the end-of-treatment and TOC visits in the micro-ITT and ME populations, the safety and tolerability of eravacycline in the safety population and pharmacokinetic parameters after eravacycline administration.

On July 25, 2017, we announced top-line data from IGNITE4. In the trial, eravacycline met the primary endpoint of statistical non-inferiority of clinical response at the TOC visit, under the guidance set by the FDA and the EMA. The primary efficacy analysis under the FDA guidance was conducted using a 12.5% non-inferiority margin in the micro-ITT population. Clinical cure rates in the micro-ITT population were 90.8% and 91.2% for eravacycline (n=195) and meropenem (n=205), respectively (95% CI: -6.3%,5.3%). Under the EMA guidance, the primary analysis was conducted using a 12.5% non-inferiority margin of the MITT and CE patient populations. Clinical cure rates in the MITT population were 92.4% and 91.6% for eravacycline (n=250) and meropenem (n=249), respectively (95% CI: -4.1%,5.8%). Clinical cure rates in the CE population were 96.9% and 96.1% for eravacycline (n=225) and meropenem (n=231), respectively (95% CI: -2.9%,4.5%). The secondary analyses were consistent with, and supportive of, the primary outcome. The most commonly reported drug-related adverse events for eravacycline were gastrointestinal, including nausea (2.4%) and emesis (1.6%). This adverse event profile for eravacycline was consistent with that seen in the phase 2 clinical trial of eravacycline in cIAI. The spectrum of pathogens in this trial was similar to that seen in other pivotal trials of antibiotics in this patient population. The most common Gram-negative pathogens in the trial included *Escherichia coli, Klebsiella pneumonia, Pseudomonas* and *Bacteroides.*

*cUTI*

Our initial phase 3 clinical trial of eravacycline for the treatment of patients with cUTI was our IGNITE2 trial. In September 2015, we announced that eravacycline did not meet the primary endpoint of statistical non-inferiority compared to levofloxacin in IGNITE2 for the treatment of cUTI.

Following the failure of eravacycline to meet the primary endpoint of IGNITE2, and based on discussions with the FDA, we determined to conduct our IGNITE3 phase 3 clinical trial evaluating the IV formulation of eravacycline in patients with cUTI and to continue our development program for an oral formulation of eravacycline.

*IGNITE3*

IGNITE3 was a phase 3 randomized, double-blind, double-dummy, multi-center, prospective study that is designed to assess the efficacy, safety and pharmacokinetics of once-daily IV eravacycline (1.5mg/kg every 24 hours) compared to ertapenem (1g every 24 hours), the control therapy in this trial, for the treatment of cUTI. We enrolled approximately 1,200 adult patients in the trial, who were randomized 1:1 to receive eravacycline or ertapenem for a minimum of 5 days and were then be eligible for transition to an approved oral agent. The co-primary endpoints of responder rate (a combination of clinical cure and microbiological success) in the micro-ITT population at the end-of-IV treatment visit and at the TOC visit (Day 5-10 post therapy) were evaluated using a 10% non-inferiority margin.

On February 13, 2018, we announced top-line data from our IGNITE3 trial. In this trial, eravacycline did not meet the co-primary endpoints of responder rate, a combination of clinical cure and microbiological success, in the micro-ITT, population at the end-of-IV treatment visit and at the test-of-cure visit.

Responder rates in the micro-ITT population at the end-of-IV treatment visit were 84.8% and 94.8% for eravacycline (n=428) and ertapenem (n=403), respectively (-10.0% CI: -14.1%, -6.0%). Responder rates at the TOC visit were 68.5% and 74.9% for eravacycline (n=428) and ertapenem (n=403), respectively (-6.5% CI: -12.6%, -0.3%). While eravacycline was well tolerated in this trial, it did not meet the co-primary endpoints. Non-inferiority to ertapenem was not demonstrated. We continue to analyze the data of this study. However, given the IGNITE3 results, we are no longer evaluating IV eravacycline for the treatment of cUTI and have also ceased development of an oral formulation for eravacycline for the treatment of cUTI.

*IGNITE2*

IGNITE2 was a two-part, multi-center, randomized, double-blind phase 3 clinical trial, our IGNITE2 trial, to assess the efficacy and safety of eravacycline compared with levofloxacin in the treatment of cUTI. We enrolled 143 patients in the lead-in portion of the trial. These patients were randomized into three arms on a 1:1:1 basis: an arm in which patients received 1.5 mg/kg IV eravacycline every 24 hours followed by 200 mg of eravacycline orally every 12 hours; an arm in which patients received 1.5 mg/kg IV eravacycline every 24 hours followed by 250 mg of eravacycline orally every 12 hours; and an arm in which patients received 750 mg IV levofloxacin every 24 hours followed by 750 mg of levofloxacin orally every 24 hours.

We enrolled 908 patients in the pivotal portion of the trial. These patients were randomized on a 1:1 basis to receive 1.5 mg/kg IV eravacycline every 24 hours followed by 200 mg of eravacycline orally every 12 hours or 750 mg IV levofloxacin every 24 hours followed by 750 mg of levofloxacin orally every 24 hours. In both treatment arms, subjects received a minimum of three days of IV therapy and then, if clinically indicated, were eligible to transition to oral therapy for the remaining doses for a total treatment period of 7 days. We designed the pivotal portion of the trial as a non-inferiority study in compliance with both FDA and EMA guidance. Under FDA guidance, the primary endpoint of the pivotal portion of the trial was clinical and microbiological response in the micro-ITT population at the PT visit. Under EMA guidance, the primary endpoint of the pivotal portion of the trial was microbiological response in the micro-MITT and ME populations. The micro-MITT population consisted of any patient who received study drug who had baseline bacterial pathogens that cause cUTI and against which eravacycline has antibacterial activity. The ME population consisted of all micro-ITT patients who met key inclusion/exclusion criteria and followed other important components of the trial. In order to achieve the primary endpoint under both FDA and EMA guidance, eravacycline would have needed to demonstrate non-inferiority as compared to levofloxacin within a margin of no more than 10%. A key secondary endpoint in IGNITE2 was to test for superiority of eravacycline over levofloxacin in the treatment of cUTI for those subjects with infections caused by quinolone-resistant pathogens by evaluation of clinical and microbiological response in the micro-ITT population at the PT visit.

In September 2015, we announced that eravacycline did not meet the primary endpoint of statistical non-inferiority compared to levofloxacin in IGNITE2 for the treatment of cUTI under the guidance set by the FDA. The primary analysis under the FDA guidance was conducted using a 10% non-inferiority margin in the micro-ITT population. In the micro-ITT population, the lower and upper bounds of the 95% confidence interval were -14.1% and 1.2%, respectively.

***Previous clinical trials of eravacycline***

*Phase 2 clinical trial of IV formulation in cIAI*

In June 2012, we completed a global, multi-center, randomized, double-blind phase 2 clinical trial to evaluate the efficacy, safety and pharmacokinetics of the IV formulation of eravacycline compared to ertapenem in patients with cIAI.

We enrolled 143 hospitalized patients with cIAI in the trial. These patients were randomized into three arms on a 2:2:1 basis: an arm in which patients received 1.5 mg/kg IV eravacycline administered once per day; an arm in which patients received 1.0 mg/kg IV eravacycline administered twice per day; and a control arm in which patients received 1.0 g IV ertapenem administered once per day, which is the standard dosing regimen for ertapenem.

Investigators obtained baseline intra-abdominal cultures at the time of operation and treated patients for a minimum of four days and a maximum of 14 days. The length of treatment for each patient was determined by the physician based on pre-set parameters. A TOC visit took place ten to 14 days after the last dose of drug was administered and a final or follow-up visit occurred within four to six weeks after the last dose of drug was administered.

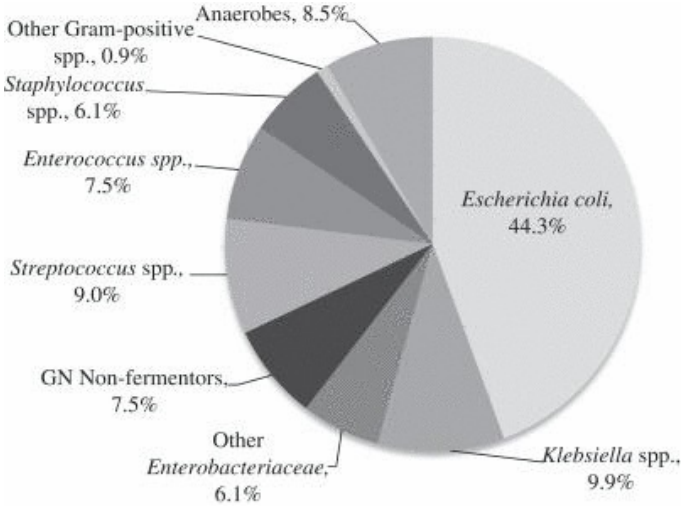
In the trial, ME patients in the eravacycline arms experienced similar infection cure rates to the ME patients in the ertapenem arm, as summarized in the table below. The table also shows the 95% confidence interval, a statistical determination that demonstrates the range of possible differences in the point estimates of success that will arise 95% of the time the endpoint is measured.

**Eravacycline Phase 2 Trial Primary Endpoint Analysis**

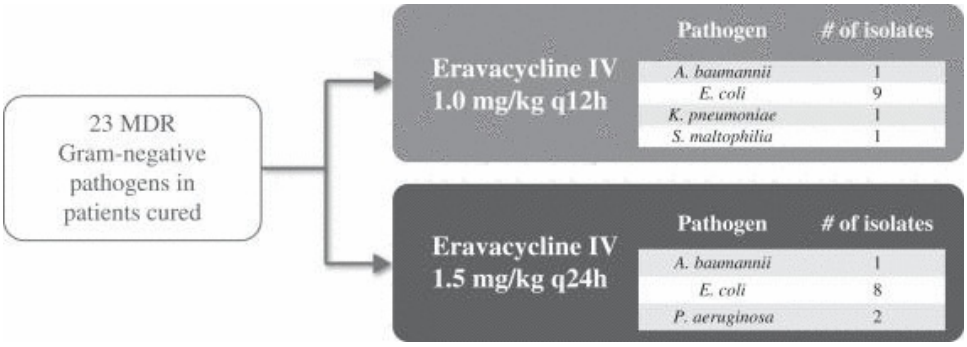
| Population | Eravacycline (1.5 mg/kg every 24 hours) | Eravacycline (1.0 mg/kg every 12 hours) | Ertapenem (1.0 g Every 24 hours) |
|---|---|---|---|
| Microbiologically Evaluable (ME) | N=42 | N=41 | N=26 |
| % Cure in ME (95% Confidence Interval) | 92.9 (80.5-98.5) | 100 (91.4-100) | 92.3 (74.9-99.1) |

Investigators in the trial had the discretion to determine the period that patients remained on the applicable treatment. The mean duration of treatment in the trial was 6.1 days for the patients receiving 1.5 mg/kg IV eravacycline administered once per day; 5.6 days for the patients receiving 1.0 mg/kg IV eravacycline administered twice per day; and 6.0 days for the patients receiving 1.0 g IV ertapenem administered once per day.

The figure below shows the overall pathogen mix identified in the phase 2 cIAI clinical trial. Of the pathogens isolated from the micro-MITT patients enrolled in the phase 2 clinical trial, approximately 60% were members of the *Enterobacteriaceae* family. Micro-MITT patients in the trial were infected with an average of 1.8 pathogens. The Gram-negative aerobic pathogens occurring most frequently were *Escherichia coli, Klebsiella pneumonia, Klebsiella oxytoca, Pseudomonas aeruginosa, Acinetobacter baumannii complex* and *Morganella morganii*. The Gram-positive aerobic pathogens occurring most frequently were *Streptococcus spp., Enterococcus faecalis* and *Staphylococcus aureus*. The anaerobic pathogens occurring most frequently were *Bacteroides fragilis* and *Clostridium spp.*




Of particular importance in the trial results was the performance of eravacycline against confirmed drug-resistant Gram-negative pathogens as well as other challenging Gram-negative pathogens. Due to the global, multi-center nature of the trial and our emphasis on sites in known geographic "hot spots" for multidrug-resistant Gram-negative bacteria, 25% of the Gram-negative pathogens identified in micro-MITT patients were confirmed to be multidrug-resistant as a result of being ESBL-positive and/or carbapenem-resistant. The figure below shows that the patients cured with eravacycline in the phase 2 cIAI clinical trial had 23 confirmed multidrug-resistant Gram-negative pathogens.




In the phase 2 clinical trial, eravacycline demonstrated a comparable safety and tolerability profile to ertapenem. No patients in the trial suffered any serious adverse events that were found to be related to eravacycline, and the percentage of patients in the trial arms that experienced treatment emergent adverse events, or TEAEs, were similar. In addition, gastrointestinal adverse events known to be associated with tetracyclines such as nausea and emesis, occurred at low rates in the eravacycline arms that were similar to the rates for the ertapenem arm. Adverse events associated with infusion sites were limited and similar in all treatment groups.

***Phase 1 clinical trials of IV formulation***

We studied the IV formulation of eravacycline in several phase 1 clinical trials in a total of 140 healthy volunteers and at doses ranging from 0.1 mg/kg to 3.0 mg/kg. No serious adverse events were reported during the phase 1 clinical trials and no clinically significant dose-related safety signals were reported. As expected in this class of antibiotics, transient gastrointestinal adverse events such as nausea and emesis were observed at the higher dose levels in the phase 1 clinical trials. Additionally, pharmacokinetic data demonstrates that eravacycline achieves high concentration levels in the blood and urine.

**TP-271**

TP-271 is a fully-synthetic, broad-spectrum fluorocycline being developed for respiratory diseases caused by bacterial biothreat pathogens under funding provided by NIAID. We are collaborating with CUBRC on the TP-271 program funded by NIAID.

We created TP-271 using our proprietary chemistry technology. In doing so, we made modifications to the tetracycline scaffold that were designed to improve potency and effectiveness against a broader spectrum of bacteria as compared to tetracycline and doxycycline, which are currently used for the treatment of pneumonia and other respiratory ailments.

In our development program for TP-271, we have conducted a number of *in vitro*, toxicology and animal studies to evaluate the efficacy of TP-271 against biothreat pathogens. TP-271 has performed as well as, or better than, standard-of-care comparators in studies in murine respiratory infection models challenged with public health pathogens. In susceptibility studies, TP-271 also demonstrated broad-spectrum activity against NIAID Category A and B public health bacterial pathogens including *Francisella tularensis, Yersinia pestis, Burkholderia mallei, Burkholderia pseudomallei, Bacillus anthracis*, and NIAID Category C public health bacterial pathogens (*in vitro* and *in vivo*) that are associated with CABP, including *Streptococcus pneumoniae*, including multidrug-resistant *pneumococci, Staphylococcus aureus* (methicillin-susceptible and methicillin-resistant), *Haemophilus influenzae, Moraxella catarrhalis* and *Legionella pneumophila*, including strains that are tetracycline-resistant.

In June 2017, we announced positive results from a phase 1 single-ascending dose clinical trial of the IV formulation of TP-271 in healthy volunteers. In the study, TP-271 was well tolerated at single doses that resulted in high plasma exposures. There were no clinically significant changes in lab values, ECG parameters, or physical exam findings. There were no serious or severe adverse events, or discontinuations due to an adverse event during the study. We are conducting a multiple-ascending dose trial for the IV formulation of TP-271. In 2017 we completed a single ascending dose phase 1 study for the oral formulation of TP-271. Using this formulation, in early 2018 we initiated a multiple-ascending dose phase 1 study for the oral formulation of TP-271. In February 2017, we also received Qualified Infectious Disease Product and Fast Track designations from the FDA.

Funding for TP-271 is covered by two awards from NIAID. The first award is a grant awarded to CUBRC in July 2011 that provides up to approximately $2.9 million in funding, which we refer to as the NIAID Grant. The second award is a contract awarded to CUBRC in September 2011 that provides up to approximately $35.8 million in funding. The NIAID Grant and the NIAID Contract each support the development, manufacturing and clinical evaluation of TP-271 for respiratory diseases caused by biothreat and antibiotic-resistant public health pathogens, including *Francisella tularensis, Yersinia pestis* and *Bacillus anthracis*, as well as bacterial pathogens associated with community-acquired bacterial pneumonia.

In connection with the NIAID Contract, in October 2011, we entered into a cost-plus-fixed-fee subcontract with CUBRC under which we may receive funding of up to approximately $16.9 million, reflecting the portion of the NIAID Contract funding that may be paid to us for our activities. In connection with the NIAID Grant, in November 2011, CUBRC awarded us a subaward of approximately $0.9 million, reflecting the portion of the NIAID Grant funding that may be paid to us for our activities.

The NIAID Grant expired in May 2017. Although the NIAID Contract and our subcontract with CUBRC under the NIAID Contract have terms which currently expire on March 31, 2019, NIAID is entitled to terminate the project for convenience at any time, and is not obligated to provide continued funding beyond March 31, 2019. To the extent that NIAID ceases to provide funding of the programs to CUBRC, CUBRC has the right to cease providing funding to us. As of December 31, 2017, committed funding from CUBRC under the subcontract with respect to the NIAID Contract and the subaward with respect to the NIAID Grant is $16.9 million, of which $13.2 million had been received through December 31, 2017. Through December 31, 2017, the Company had received all committed funding of $0.9 million from CUBRC under the Company's subaward with respect to the NIAID Grant.

**TP-6076**

TP-6076, a fully-synthetic fluorocycline derivative, is the lead candidate under our second-generation program to target unmet medical needs, including multidrug-resistant Gram-negative bacteria. In June 2017, we announced positive results from a phase 1 randomized, placebo-controlled, double-blind, single-ascending dose study evaluating the safety, tolerability and pharmacokinetics

of IV TP-6076. In the study, TP-6076 was well tolerated, and there were no serious or severe adverse events, or discontinuations due to an adverse event. There were no clinically significant safety findings in any laboratory assessments, vital signs, ECGs or physical examinations. We also are conducting a multiple-ascending study in healthy volunteers of the IV formulation of TP-6076.

Funding for TP-6076 is partially covered by an award from CARB-X. In March 2017, CARB-X selected us to receive up to $4.0 million in research funding over eighteen months for TP-6076. In connection with this funding, we entered into a cost reimbursement Sub-Award Agreement or "Sub-Award Agreement", with the Trustees of Boston University, the administrator of the program. We began recognizing revenue from the Sub-Award Agreement in April 2017. During the year ended December 31, 2017, we recognized revenue of $0.7 million under this Sub-Award Agreement. This Sub-Award Agreement will fund certain activities through the end of 2018. This Sub-Award Agreement can be terminated for convenience at any time, subject to 30 days prior written notice.

**Commercialization Strategy**

Our commercialization strategy is to develop our product candidates into leading therapies that will be available worldwide for the treatment of serious multidrug-resistant infections. We have retained worldwide commercial rights to all of our product candidates other than eravacycline in China and other Asian territories. We exclusively licensed our commercial rights in China and other Asian territories to Everest Medicines Limited in February 2018. In the future we may enter into additional regional licensing transactions similar to the Everest license agreement. We intend to retain control over the commercial execution of each of our product candidates in the United States.

We are currently developing our lead product candidate, eravacycline, as an IV antibiotic for use as a first-line empiric monotherapy for the treatment of serious and life-threatening infections, including a wide variety of multidrug-resistant infections, such as those found in patients with cIAI. We intend to directly commercialize eravacycline in the United States. We intend to build a commercial organization in the United States, and recruit experienced sales and medical education professionals and to develop a commercial strategy to target institutions with the greatest use of drugs for multidrug-resistant serious and life-threatening infections. We expect that our sales force will focus on educating hospital and institution-based physicians, nurses, pharmacy directors and payers about the benefits of eravacycline for the product's approved indications. We plan to commercialize eravacycline outside the United States with the assistance of collaborators.

**Manufacturing and Supply**

We do not own or operate manufacturing facilities for the production of any of our product candidates, nor do we have plans to develop our own manufacturing operations in the foreseeable future. All of our product candidates are organic compounds of low molecular weight, commonly referred to as small molecules. They are manufactured in a fully synthetic process from readily available starting materials.

We currently rely on a limited number of third-party contract manufacturers for all of our required raw materials, drug substance and finished product for our preclinical research and clinical trials. We do not have long-term agreements with any of these third parties. We also do not have any current contractual relationships for the manufacture of commercial supplies of any of our product candidates after they are approved. If any of our products are approved by any regulatory agency, we intend to enter into agreements with third-party contract manufacturers for the commercial production of those products. We currently employ internal resources to manage our manufacturing.

*Patheon UK Limited Master Manufacturing Services Agreement*

In June 2017, we and Patheon UK Limited and certain of its affiliates, or Patheon, entered into a master manufacturing services agreement, or the Patheon agreement. Under the Patheon agreement, we are responsible for supplying the active pharmaceutical ingredient for eravacycline to Patheon, and Patheon is responsible for manufacturing eravacycline, conducting quality control, quality assurance, analytical testing and stability testing and packaging. We entered into two related product agreements pursuant to the Patheon agreement that govern the terms and conditions of Patheon's manufacture of commercial supplies of eravacycline at Patheon's Greenville, North Carolina and Ferentino, Italy manufacturing sites. Each product agreement is governed by the terms of the Patheon agreement, unless expressly modified in such product agreement. Pursuant to the Patheon agreement, we have agreed to order from Patheon at least a certain percentage of our annual commercial requirements for eravacycline in the United States and European Union each year for the term of the Patheon agreement.

The Patheon agreement has an initial term ending December 31, 2022, and will automatically renew after the initial term for successive terms of two years each, unless either party gives notice of its intention to terminate at least 18 months prior to the end of the then current term. We may terminate a product agreement upon 30 days' prior written notice if any governmental agency takes any

action that prevents us from importing, exporting, purchasing or selling eravacycline. Either party may terminate the Patheon agreement or a product agreement (a) upon written notice if the other party has failed to remedy a material breach under the Patheon agreement or a product agreement within a specified time following receipt of written notice of such breach, and (b) immediately upon written notice to the other party in the event that the other party is declared insolvent or bankrupt, a voluntary petition of bankruptcy is filed in any court by such other party or the Pantheon agreement or a product agreement is assigned by such other party for the benefit of creditors. Patheon may terminate the Patheon agreement or a product agreement upon six months written notice if we assign the Patheon agreement to an assignee that, in the opinion of Patheon acting reasonably, is (i) not a creditworthy substitute for us or (ii) a competitor of Patheon.

The Patheon agreement contains, among other provisions, customary representations and warranties by the parties, a grant to Patheon of certain limited license rights to our intellectual property in connection with Patheon's performance of the services under the Patheon agreement, certain indemnification rights in favor of both parties, limitations of liability and customary confidentiality provisions.

*Finorga SAS Commercial Supply Agreement*

In October 2017, we and Finorga SAS, or Novasep entered into a Commercial Supply Agreement, or the Novasep agreement. Under the Novasep agreement, Novasep will, pursuant to accepted purchase orders entered into under the Novasep agreement, manufacture for commercial supply the active pharmaceutical ingredient, or API, for eravacycline for us.

Under the Novasep agreement, we will submit to Novasep on a periodic basis on or before the first business day of each calendar quarter a rolling forecast for a certain time period that sets forth the total quantity of the API for eravacycline for commercial supply that we either have ordered, desire to order or expect to order from Novasep. A certain time period of each such forecast is binding on us and constitutes a "firm order". The remainder of each forecast will be for planning purposes only, and will not be binding. Novasep has no obligation to manufacture the API for eravacycline in accordance with any forecast that is not the subject of a firm order and which is increased by a certain percentage above the previously forecast amount.

The Novasep agreement has an initial term ending October 16, 2022, and will automatically renew after the initial term, unless either party gives notice of its intention to terminate at least 18 months prior to the end of the then current term. We may terminate the Novasep agreement upon 30 days' prior written notice (a) if any regulatory authority takes any action, or raises any objection, that prevents us from importing, exporting, purchasing or selling the API for eravacycline, or (b) in the event that Novasep experiences a force majeure event. Either party may terminate the Novasep agreement (a) upon written notice if the other party has failed to remedy a material breach under the Novasep agreement within a specified time following receipt of written notice of such breach, and (b) immediately upon written notice to the other party in the event the other party makes a general assignment for the benefit of its creditors, or proceedings of a case are commenced in any court of competent jurisdiction by or against the other party seeking (i) such party's reorganization, liquidation, dissolution, arrangement or winding up, or the composition or readjustment of its debts, (ii) the appointment of a receiver or trustee for or over such party's property, or (iii) similar relief in respect of such party under any law relating to bankruptcy, insolvency, reorganization, winding up or composition or adjustment of debt, and such proceedings shall continue undismissed, or an order with respect to the foregoing shall be entered and continue unstayed, for a period of more than 60 days.

The Novasep agreement contains, among other provisions, customary representations and warranties by the parties, a grant to Novasep of certain limited license rights to the Company's intellectual property in connection with Novasep's performance of the services under the Novasep agreement, certain indemnification rights in favor of both parties, limitations of liability and customary confidentiality provisions.

**Intellectual Property**

We strive to protect the proprietary technology that we believe is important to our business, including seeking and maintaining patents intended to cover our product candidates and compositions, their methods of use and processes for their manufacture and any other inventions that are commercially important to the development of our business. We also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

Our success will significantly depend on our ability to obtain and maintain patent and other proprietary protection for commercially important technology and inventions and know-how related to our business, defend and enforce our patents, preserve the confidentiality of our trade secrets and operate without infringing the valid and enforceable patents and proprietary rights of third parties. We also rely on know-how and continuing technological innovation to develop and maintain our proprietary position.

As of February 26, 2018, we owned nine U.S. patents, 42 foreign patents, seven pending U.S. patent applications, three pending applications filed under the Patent Cooperation Treaty, or PCT, and 62 pending foreign patent applications in Europe and 20 other jurisdictions. The PCT is an international patent law treaty that provides a unified procedure for filing a single initial patent application for an invention simultaneously in each of the member states. Although a PCT application is not itself examined and cannot issue as a patent, it allows the applicant to seek protection in any of the member states through national-phase applications. In addition, we have exclusively licensed from Harvard University rights under 12 U.S. patents, 30 foreign patents, one pending U.S. patent application and eight pending foreign patent applications in Europe and ten other jurisdictions. Certain of our patents and patent applications are directed to the composition of matter and/or use of eravacycline and patents have granted or applications are pending in the United States, Europe, Japan and other countries.

***Tetraphase-Owned Intellectual Property Relating to Eravacycline and Other Compounds Under Development***

We have patent applications directed to the composition of matter and/or use of eravacycline and other fluorocyclines pending in the United States and other countries. Patents specific to the composition of matter, pharmaceutical compositions and/or use of eravacycline have been granted in the United States, Europe, Australia, China, Colombia, India, Japan, Korea, Mexico, New Zealand, Hong Kong, Taiwan, Israel and Singapore. The granted patents have an expiration date of August 7, 2029, and any patents that may issue from the pending applications will also have an expiration date of August 7, 2029, absent any term extensions or adjustments that may be available. The term of one of the U.S. patents has received 508 days of patent term adjustment under the America Invents Act.

We have also filed patent applications directed to the composition of matter and use of various derivatives of tetracycline and pentacycline (a tetracycline scaffold extended to five rings) under the PCT and in the United States, Europe and other foreign countries. Any patents that might issue from these pending applications will have an expiration date no earlier than 2030, with some expiration dates as late as 2038.

***Exclusively Licensed Intellectual Property Relating to Our Proprietary Chemistry Technology***

The patents and patent applications that we exclusively license from Harvard provide patent protection for the proprietary chemistry technology used in our fully synthetic process to make eravacycline and other tetracycline derivatives. The key intermediates that enable our fully synthetic process are commonly referred to as enone intermediates. The licensed patents and patent applications are directed towards the composition of matter of enone intermediates and compounds used to make the enone intermediates, referred to as key precursors, as well as synthetic routes to those enone intermediates, precursors and our tetracycline derivatives under development.

Composition of matter for the enone intermediates and precursors used in preparing the enone intermediates, and methods of making the precursors and enone intermediates are covered by the U.S. patents we license from Harvard, which will expire no earlier than 2025, not taking into consideration patent term adjustment. Corresponding patent applications have been filed in foreign jurisdictions and any patents that have issued and might issue from these applications also expire or will expire no earlier than 2025.

***Exclusively Licensed Intellectual Property Relating to Pentacycline and Tetracycline Derivatives***

Our license from Harvard also includes patent applications directed to the composition of matter and use of other novel tetracycline or pentacycline derivatives. These applications are pending in the United States, Europe and other countries. Any patents that might issue from these pending applications will have an expiration date no earlier than 2027.

***Patent Term and Patent Term Extensions***

The term of individual patents depends upon the legal term for patents in the countries in which they are obtained. In most countries, including the United States, the patent term is 20 years from the earliest filing date of a non-provisional patent application. In the United States, a patent's term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the U.S. Patent and Trademark Office in examining and granting a patent, or may be shortened if a patent is terminally disclaimed over an earlier filed patent. The term of a patent that covers a drug, biological product or medical device approved pursuant to a pre-market approval may also be eligible for patent term extension when FDA approval is granted, provided statutory and regulatory requirements are met. The length of the patent term extension is related to the length of time the drug is under regulatory review while the patent is in force. The Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, permits a patent term extension of up to five years beyond the expiration date set for the patent. Patent extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent applicable to each regulatory review period may be granted an extension and only those claims reading on the approved drug are extended. Similar provisions are available in Europe and other foreign jurisdictions to extend the term of a patent that covers an approved drug.

***Trademark Applications Relating to the Company Name and Logo***

As of February 1, 2018, we owned ten intent-to-use trademark applications pending before the United States Patent and Trademark Office relating to the Company Name, the Company Logo, combinations thereof, design marks relating to eravacycline and potential commercial names of eravacycline.

***Trade Secrets***

We rely, in some circumstances, on trade secrets to protect our unpatented technology. However, trade secrets can be difficult to protect. We seek to protect our trade secrets and proprietary technology and processes, in part, by confidentiality agreements with our employees, consultants, scientific advisors and contractors. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, agreements or security measures may be breached. We may not have adequate remedies for any breach and could lose our trade secrets through such a breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our consultants, contractors or collaborators use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting trade secrets, know-how and inventions.

**Harvard University License Agreement**

On August 3, 2006, we entered into a license agreement with The President and Fellows of Harvard College, under which Harvard granted us an exclusive worldwide license under specified Harvard patent rights to develop and commercialize tetracycline-based products such as eravacycline. Under the license agreement, we also have the right to expand the patent rights subject to the license to include improvement patents that may be owned by Harvard in the future and that meet specified criteria by paying to Harvard an additional license issuance fee in an amount to be agreed between Harvard and us. We also have a right of negotiation to expand the license to include additional patents relating to tetracycline chemistry within a specified category that may be owned by Harvard in the future, including patents covering inventions made by Andrew Myers, Ph.D., our scientific founder, under his consulting agreement with us. Since entering into the license agreement, we have entered into amendments to the license agreement pursuant to which we expanded the patent rights subject to the license in accordance with these rights. Under the license agreement, we are obligated to satisfy diligence requirements, including using commercially reasonable efforts to develop and commercialize licensed compounds and to implement a specified development plan, meeting specified development milestones and providing an update on progress on an annual basis. Our license grant from Harvard is subject to academic rights retained by Harvard and United States government rights and obligations that are customary in patent license agreements with universities in the United States.

In consideration for the rights granted to us by Harvard under the license agreement, as of December 31, 2017, we have paid Harvard an aggregate of $6.1 million in upfront license fees and development milestone payments, and issued 31,379 shares of our common stock to Harvard. In addition, we have agreed to make payments to Harvard upon the achievement of specified future development and regulatory milestones totaling up to $15.1 million for each licensed product candidate ($4.8 million of which has already been paid with respect to eravacycline), and to pay tiered royalties in the single digits based on annual worldwide net sales, if any, of licensed products by us, our affiliates and sublicensees in certain circumstances. We are also obligated to pay Harvard a specified share of non-royalty sublicensing and other revenues that we receive from sublicensees for the grant of sublicenses under the license in certain circumstances, and to reimburse Harvard for specified patent prosecution and maintenance costs.

The license agreement expires on a licensed product-by-licensed product and country-by-country basis upon the expiration of the last-to-expire patent covering the applicable product in the applicable country that is included in the license. Harvard may terminate the license agreement based on our uncured material breach or insolvency or bankruptcy. We have the right to terminate the license agreement for any or no reason at any time on sixty (60) days prior written notice to Harvard.

**Government Contracts**

***Eravacycline***

We received funding for eravacycline under an award from BARDA. In January 2012, BARDA awarded to CUBRC a five-year contract that provided a total of up to $67.3 million in funding. The BARDA Contract contemplates that CUBRC will collaborate with us on the development, manufacturing and clinical evaluation of a novel tetracycline antibiotic with potential as an empiric countermeasure for respiratory diseases caused by biothreat and antibiotic-resistant public health pathogens, including *Francisella tularensis*, which causes tularemia, *Yersinia pestis*, which causes plague, and *Bacillus anthracis*, which causes anthrax disease, as well as bacterial pathogens associated with moderate-to-severe CABP and other serious hospital infections. The BARDA Contract also provided funding for certain activities in the development of eravacycline to treat certain infections caused by life-threatening multidrug-resistant bacteria. In connection with the BARDA Contract, in February 2012, we entered into a cost-plus-fixed-fee subcontract with CUBRC under which we can receive up to $41.9 million to fund specific work performed by us related to eravacycline. The terms of the subcontract expire on December 31, 2018.

We collaborated with CUBRC in seeking government funding of this development program because we did not have any expertise in bidding for, or the administration and management of, government-funded contracts. Because CUBRC had the expertise to manage and administer awards issued by government funding agencies, we agreed with CUBRC that CUBRC would serve as the prime contractor under the BARDA Contract, primarily carrying out a program management and administrative role with additional responsibility for the management of certain preclinical studies. We serve as lead technical experts on all aspects of the BARDA Contract and serve as a subcontractor of CUBRC responsible for management of chemistry, manufacturing and control activities and clinical studies. The flow of funds under this arrangement follows the respective activities being conducted by us and by CUBRC, with funds being paid to us under our subcontract with CUBRC reflecting payment for our activities.

We have agreed upon a research plan with CUBRC detailing the activities to be conducted by CUBRC and by us. In addition to our obligations to conduct the activities provided for by the research plan, we are also obligated under the CUBRC subcontract to satisfy various federal reporting requirements, extending to technical reporting with respect to our activities, reporting with respect to intellectual property and financial reporting.

Payments under our subcontract with CUBRC are made in installments as activities are conducted in accordance with the research plan. Payments are based on direct and indirect costs incurred plus fixed fees, where applicable.

Under the subcontract, CUBRC's use of our eravacycline data is expressly limited to purposes of performing CUBRC's obligations under the BARDA Contract, and CUBRC and its other subcontractors must assign to us, subject to government rights, all intellectual property rights relating to our compounds and related data that arise from the project. Under standard government contracting terms, the government receives only limited rights for government use of certain of our pre-existing data and certain data produced with non-federal funding, to the extent such data are required for delivery to BARDA under the project. The government receives unlimited rights to use and disclose new data first produced under the project with BARDA funding, and the government is entitled to at least a nonexclusive, worldwide, royalty-free license to practice or have practiced any patent on an invention that is conceived or first reduced to practice under the project.

BARDA is entitled to terminate the project for convenience at any time, and is not obligated to provide continued funding beyond current-year amounts from Congressionally approved annual appropriations, and CUBRC has a right to terminate its subcontract with us only to the extent that BARDA first cancels the corresponding portions of CUBRC's prime contract.

We retain a right to terminate CUBRC's rights to use eravacycline. Permissible grounds for such termination of CUBRC's rights include but are not limited to the sale of our assets relating to the project, an acquisition of us or our granting an exclusive or partially exclusive license to use eravacycline to a licensee that declines to continue CUBRC's license rights. In such an event, the subcontract may be terminated upon CUBRC's negotiation of a corresponding termination of CUBRC's obligations to BARDA.

***TP-271***

Our program to develop TP-271 is funded by NIAID through the NIAID Grant, a grant awarded in July 2011 that provided up to approximately $2.9 million in funding, and the NIAID Contract, a separate agreement that provides up to $35.8 million in funding that NIAID awarded to CUBRC in October 2011. The NIAID Contract and the NIAID Grant contemplate that CUBRC will collaborate with us on the development, manufacturing and clinical evaluation of a novel broad-spectrum tetracycline antibiotic for respiratory diseases caused by biothreat and antibiotic-resistant public health pathogens, including *Francisella tularensis, Yersinia pestis* and *Bacillus anthracis*, as well as bacterial pathogens associated with CABP.

In connection with the NIAID Contract, in October 2011, we entered into a subcontract with CUBRC under which we may receive funding of up to approximately $16.9 million, reflecting the portion of the NIAID Contract funding that may be paid to us for our activities. The term of the NIAID subcontract now runs through March 31, 2019. In connection with the NIAID Grant, in November 2011, CUBRC awarded us a subaward of approximately $0.9 million, reflecting the portion of the NIAID Grant funding that may be paid to us for our activities. The term of the sub-award under the NIAID grant expired in May 2017.

We collaborated with CUBRC in seeking government funding of this development program because we did not have any expertise in bidding for, or the administration and management of, government-funded contracts. Because CUBRC had the expertise to manage and administer awards issued by government funding agencies, we agreed with CUBRC that CUBRC would serve as the prime contractor under the NIAID Contract, primarily carrying out a program management and administrative role with additional responsibility for the management of certain preclinical studies. We serve as lead technical experts on all aspects of the NIAID Contract and serve as a subcontractor of CUBRC responsible for management of chemistry, manufacturing and control activities and clinical studies. The flow of funds under this arrangement follows the respective activities being conducted by us and by CUBRC, with funds being paid to us under our subcontract with, and subaward from, CUBRC reflecting payment for our activities.

We have agreed upon a research plan with CUBRC detailing the activities to be conducted by CUBRC and by us. In addition to our obligations to conduct the activities provided for by the research plan, we are also obligated under the CUBRC subcontract to satisfy various federal reporting requirements, extending to technical reporting with respect to our activities, reporting with respect to intellectual property and financial reporting.

Payments under our subcontract with CUBRC are made in installments as activities are conducted in accordance with the research plan. Payments are based on direct and indirect costs incurred plus fixed fees, where applicable.

Under the subcontract, CUBRC's use and disclosure of our proprietary data pertaining to the project are expressly subject to a separate confidentiality agreement between CUBRC and us. CUBRC and its other subcontractors or subawardees must assign to us, subject to government rights, all intellectual property rights relating to our compounds and related data that arise from the project. Under standard government contracting terms and grant conditions, the government is entitled to at least a nonexclusive, worldwide, royalty-free license to practice or have practiced any patent on an invention that is conceived or first reduced to practice under the project.

NIAID is entitled to terminate the NIAID Contract for convenience at any time, and is not obligated to provide continued funding beyond March 31, 2019 and CUBRC has a right to terminate its subcontract with, or subaward to, us only to the extent that NIAID first cancels the corresponding portions of CUBRC's prime contract or award.

We retain rights to terminate the subcontract if CUBRC breaches the subcontract, subject in certain cases to CUBRC's failure to cure such breach, or by written notice to CUBRC, effective upon CUBRC's negotiation of a corresponding termination of CUBRC's obligations to NIAID.

***TP-6076***

Our program to develop TP-6076 is partially covered by an award from CARB-X. In March 2017, CARB-X selected the Company to receive up to $4.0 million in research funding over eighteen months for TP-6076. In connection with this funding, the Company entered into a cost reimbursement Sub-Award Agreement (the "Sub-Award Agreement") with the Trustees of Boston University, the administrator of the program. This Sub-Award Agreement will fund certain activities through the end of 2018. This Sub-Award Agreement can be terminated for convenience at any time, subject to 30 days prior written notice.

**Collaborations**

In February 2018, we entered into a license agreement, which we call the Everest license agreement, with Everest Medicines Limited, or Everest Medicines, whereby we granted Everest Medicines an exclusive license to develop and commercialize eravacycline, for the treatment of complicated intra-abdominal infections and other indications, in mainland China, Taiwan, Hong Kong, Macau, South Korea and Singapore, or the territory.

Under the terms of the Everest license agreement, we are eligible to receive from Everest Medicines an upfront cash payment of $7.0 million to be paid within 15 business days of the effective date of the Everest license agreement, and up to an aggregate of $16.5 million in clinical development and regulatory milestone payments and up to $20.0 million annually, provided that certain sales thresholds are met. There can be no guarantee that any such milestones or sales thresholds will in fact be met. We are obligated to make certain payments to Harvard based on amounts received from Everest Medicines under the Everest license agreement pursuant to the existing license agreement by and between Harvard and us.

We will also be entitled to receive double-digit tiered royalties on sales in the territory, if any, of products containing eravacycline. Royalties are payable with respect to each jurisdiction in the territory until the latest to occur of: (i) the last-to-expire of specified patent rights in such jurisdiction in the territory; (ii) expiration of marketing or regulatory exclusivity in such jurisdiction in the territory; or (iii) ten (10) years after the first commercial sale of a product in such jurisdiction in the territory. In addition, royalties payable under the Everest license agreement will be subject to reduction on account of generic competition and after patent expiry in a jurisdiction if required by applicable law, with any such reductions capped at certain percentages of the amounts otherwise payable during the applicable royalty payment period.

Under the terms and conditions of the Everest license agreement, Everest Medicines will be solely responsible for the development and commercialization of licensed products in the territory.

If either we or Everest Medicines materially breaches the Everest license agreement and does not cure such breach within 90 days (or fewer days in certain cases), the non-breaching party may terminate the Everest license agreement in its entirety. However,

if the breach relates only to any jurisdiction other than mainland China, the non-breaching party may only terminate the Everest license agreement with respect to such jurisdiction. Either party may also terminate the Everest license agreement, effective immediately upon written notice, if the other party files for bankruptcy, is dissolved or has a receiver appointed for substantially all of its property. We may terminate the Everest license agreement if Everest Medicines, its affiliates or its sublicensees challenges the validity or enforceability of any of our patents covering any of the licensed compounds or products. In certain circumstances, if we materially breaches the Everest license agreement Everest Medicines may reduce royalties owed to us in lieu of a termination. Moreover, if we materially breaches the Everest license agreement and Everest Medicines terminates the Everest license agreement with respect to any jurisdiction and we then commercializes a licensed product in that jurisdiction, we will pay to Everest Medicines a low, single digit royalty on such sales of the licensed product in such jurisdiction for a minimum of five years after such termination.

**Research and Development Expenses**

For the years ended December 31, 2017, 2016 and 2015, we incurred $101.7 million, $63.8 million, and $73.8 million, respectively, in expenses on research and development activities.

**Competition**

The biopharmaceutical industry is characterized by intense competition and rapid innovation. Our potential competitors include large pharmaceutical and biotechnology companies, specialty pharmaceutical companies and generic drug companies. Many of our potential competitors have greater financial, technical and human resources than we do, as well as greater experience in the discovery and development of product candidates, obtaining FDA and other regulatory approvals of products and the commercialization of those products. Accordingly, our potential competitors may be more successful than us in obtaining FDA approval for drugs and achieving widespread market acceptance. We anticipate that we will face intense and increasing competition as new drugs enter the market and advanced technologies become available. Finally, the development of new treatment methods for the diseases we are targeting could render our product candidates less competitive or obsolete.

We believe the key competitive factors that will affect the development and commercial success of our most advanced product candidate, eravacycline, if approved, will be efficacy, coverage of drug-resistant strains of bacteria, safety and tolerability profile, reliability, convenience of dosing, price, availability of reimbursement from governmental and other third-party payers and susceptibility to drug resistance.

We are developing eravacycline as an IV antibiotic for use as a first-line empiric monotherapy for the treatment of resistant and multidrug-resistant infections such as those found in patients with cIAI. If approved, eravacycline would compete with a number of currently marketed antibiotics, including meropenem, which is marketed by AstraZeneca as Merrem, imipenem/cilastatin, which is marketed by Merck & Co., or Merck, as Primaxin, tigecycline, which is marketed by Pfizer as Tygacil, piperacillin/tazobactam, which is marketed by Pfizer as Zosyn, ceftolozane/tazobactam, which is marketed by Merck as Zerbaxa, and ceftazidime/avibactam, which is marketed by Allergan, Inc., and AstraZeneca as Avycaz, meropenem and vaborbactam, which is marketed by Melinta Therapeutics as Vabomere, as well as several antibiotics currently in phase 3 development. We also expect that eravacycline, if approved, would compete with future and current generic versions of marketed antibiotics.

If approved, we believe that eravacycline would compete effectively against these compounds on the basis of:

- broad range of activity against a wide variety of resistant and multidrug-resistant Gram-negative, Gram-positive and anaerobic bacteria;
- lower probability of drug resistance;
- a favorable safety and tolerability profile;
- a convenient dosing regimen;
- allows for monotherapy; and
- no drug to drug interactions

**Recent Changes in the Regulatory Landscape**

The FDA's Division of Anti-Infective Products, or DAIP, has undergone evolution in recent years, primarily driven by concerns that increasingly less effective antibiotics may have been approved in the last 10 to 15 years and a desire to bring what DAIP perceives to be greater statistical rigor to their analyses. The impact of this was a rethinking of how antibiotic efficacy is measured in clinical trials, and a review of the statistical tools used to analyze the data. In February 2015, the FDA published guidance documents for industry entitled "Complicated Urinary Tract Infections: Developing Drugs for Treatment" and guidance entitled "Complicated Intra-Abdominal Infections: Developing Drugs for Treatment." The purpose of these guidance documents was to address considerations surrounding the clinical development of drugs for cUTI and cIAI indications, including clinical trial design and efficacy considerations.

On December 13, 2016, President Obama signed into law the 21st Centuries Cures Act, which builds on the FDA's ongoing efforts to advance medical product innovation. One key component of this Act is the Limited Population pathway, which is designed to help streamline the development programs for certain antibacterials intended to treat targeted groups of patients suffering from serious or life-threatening infections where unmet need exists due to lack of available therapies. Approvals of these antimicrobials are expected to rely on data primarily targeting these limited populations. The statement "Limited Population" will appear prominently next to the drug's name in labeling, which will provide notice to healthcare providers that the drug is indicated for use in a limited and specific population of patients. There is additional legislation pending in the U.S. Congress, including the DISARM Act, which would designate certain novel antibiotics used to treat serious bacterial infections to receive higher Medicare reimbursement, and an amendment to the GAIN Act, which would successful QIDP sponsors to transfer up to one year exclusivity to another product, including products marketed by other companies.

**Government Regulation and Product Approval**

Government authorities in the United States, at the federal, state and local level, and in other countries, extensively regulate, among other things, the research, development, clinical trials, testing, manufacture, including any manufacturing changes, authorization, pharmacovigilance, adverse event reporting, recalls, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, import and export of pharmaceutical products and product candidates such as those we are developing. The processes for obtaining regulatory approvals in the United States and in foreign countries, along with subsequent compliance with applicable statutes and regulations, require the expenditure of substantial time and financial resources.

***U.S. Government Regulation***

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant to a variety of administrative or judicial sanctions, such as the FDA's refusal to approve pending NDAs, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil and/or criminal penalties.

The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practice, or GLP, regulations;
- submission to the FDA of an IND which must become effective before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, at each clinical site before each trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practices, or GCP, to establish the safety and efficacy of the proposed drug product for each indication;
- submission to the FDA of an NDA;
- satisfactory completion of an FDA advisory committee review, if applicable;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with current good manufacturing practices, or cGMP, and to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity; and
- FDA review and approval of the NDA.

*Preclinical Studies*

Preclinical studies include laboratory evaluation of product chemistry, toxicity and formulation, as well as animal studies to assess potential safety and efficacy. Preclinical tests intended for submission to the FDA to support the safety of a product candidate must be conducted in compliance with the FDA's Good Laboratory Practice (GLP) regulations and the United States Department of Agriculture's Animal Welfare Act. A drug sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data and any available clinical data or literature, among other things, to the FDA as part of an IND. Some preclinical testing may continue even after the IND is submitted. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the clinical trial on a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing clinical trials to commence.

*Clinical Trials*

Clinical trials involve the administration of the investigational new drug to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include the requirement that all research subjects provide their informed consent in writing for their participation in any clinical trial along with the requirement to ensure that the data and results reported from the clinical trials are credible and accurate. Clinical trials are conducted under protocols detailing, among other things, the objectives of the trial, the criteria for determining subject eligibility, the dosing plan, the parameters to be used in monitoring safety, the procedure for timely reporting of adverse events, and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, an IRB at each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution. Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health, or NIH, for public dissemination on their www.clinicaltrials.gov website.

Human clinical trials are typically conducted in three sequential phases, which may overlap or be combined:

Phase 1: The drug is initially introduced into healthy human subjects or patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness. During phase 1 clinical trials, sufficient information about the investigational drug's or biological product's pharmacokinetics and pharmacological effects may be obtained to permit the design of well-controlled and scientifically valid phase 2 clinical trials.

Phase 2: The drug is administered to a larger, but still limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted indications and to determine dosage tolerance and optimal dosage. Phase 2 clinical trials are typically well-controlled and closely monitored.

Phase 3: The drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product, and to provide adequate information for the labeling of the product. Phase 3 clinical trials usually involve a larger number of participants than a phase 2 clinical trial.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur. Phase 1, phase 2 and phase 3 clinical trials may not be completed successfully within any specified period, or at all. Results from one trial may not be predictive of results from subsequent trials. Furthermore, the FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients.

*Special Protocol Assessment*

The special protocol assessment, or SPA, process is designed to facilitate the FDA's review and approval of drugs by allowing the FDA to evaluate the proposed design and size of phase 3 clinical trials that are intended to form the primary basis for determining a drug product's efficacy. Generally, the trial must have already been discussed with the relevant FDA review division at an end-of-phase 2/pre-phase 3 meeting to be eligible for SPA review. Upon specific request by a clinical trial sponsor, the FDA will evaluate the protocol and respond to a sponsor's questions regarding, among other things, primary efficacy endpoints, trial conduct and data analysis, within 45 days of receipt of the request.

The FDA ultimately assesses whether the protocol design and planned analysis of the trial are acceptable to support regulatory approval of the product candidate with respect to effectiveness of the indication studied. All agreements and disagreements between the FDA and the sponsor regarding an SPA must be clearly documented in an SPA letter or the minutes of a meeting between the sponsor and the FDA.

Even if the FDA agrees to the design, execution and analyses proposed in protocols reviewed under the SPA process, the FDA may revoke or alter its agreement under the following circumstances:

- public health concerns emerge that were unrecognized at the time of the protocol assessment, or the director of the review division determines that a substantial scientific issue essential to determining safety or efficacy has been identified after testing has begun;
- a sponsor fails to follow a protocol that was agreed upon with the FDA; or
- the relevant data, assumptions, or information provided by the sponsor in a request for SPA change are found to be false statements or misstatements, or are found to omit relevant facts.

A documented SPA may be modified, and such modification will be deemed binding on the FDA review division, except under the circumstances described above, if FDA and the sponsor agree in writing to modify the protocol and such modification is intended to improve the study.

*Marketing Approval*

Assuming successful completion of the required clinical testing, the results of the preclinical and clinical studies, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the product for one or more indications. In most cases, the submission of an NDA is subject to a substantial application user fee. Under the Prescription Drug User Fee Act, or PDUFA, guidelines that are currently in effect, the FDA has a goal of ten months from the date of "filing" of a standard NDA for a new molecular entity to review and act on the submission. This review typically takes twelve months from the date the NDA is submitted to FDA because the FDA has approximately two months to make a "filing" decision. Furthermore, the FDA is not required to complete its review within the established ten-month timeframe and may extend the review process by issuing requests for additional information or clarification. The PDUFA goal date for the FDA to complete its review of our NDA is currently August 28, 2018.

In addition, under the Pediatric Research Equity Act of 2003, as amended and reauthorized, certain NDAs or supplements to an NDA must contain data that are adequate to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements.

Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation. Our product candidates are not designated as orphan drugs.

The FDA also may require submission of a risk evaluation and mitigation strategy, or REMS, plan to mitigate any identified or suspected serious risks. The REMS plan could include medication guides, physician communication plans, assessment plans, and elements to assure safe use, such as restricted distribution methods, patient registries, or other risk minimization tools.

The FDA conducts a preliminary review of all NDAs within the first 60 days after submission, before accepting them for filing, to determine whether they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA reviews an NDA to determine, among other things, whether the drug is safe and effective and whether the facility in which it is manufactured, processed, packaged or held meets standards designed to assure the product's continued safety, quality and purity.

The FDA is required to refer an application for a novel drug to an advisory committee or explain why such referral was not made. An advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical trial sites to assure compliance with GCP.

The FDA generally accepts data from foreign clinical trials in support of an NDA if the trials were conducted under an IND. If a foreign clinical trial is not conducted under an IND, the FDA nevertheless may accept the data in support of an NDA if the study was conducted in accordance with GCPs and the FDA is able to validate the data through an on-site inspection, if deemed necessary. Although the FDA generally requests that marketing applications be supported by some data from domestic clinical studies, the FDA may accept foreign data as the sole basis for marketing approval if (1) the foreign data are applicable to the U.S. population and U.S. medical practice, (2) the studies were performed by clinical investigators with recognized competence, and (3) the data may be considered valid without the need for an on-site inspection or, if the FDA considers the inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means.

The testing and approval process for an NDA requires substantial time, effort and financial resources, and each may take several years to complete. Data obtained from preclinical and clinical testing are not always conclusive and may be susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. The FDA may not grant approval on a timely basis, or at all.

After evaluating the NDA and all related information, including the advisory committee recommendation, if any, and inspection reports regarding the manufacturing facilities and clinical trial sites, the FDA may issue an approval letter, or, in some cases, a complete response letter. A complete response letter generally contains a statement of specific conditions that must be met in order to secure final approval of the NDA and may require additional clinical or preclinical testing in order for FDA to reconsider the application. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when those conditions have been met to the FDA's satisfaction, the FDA will typically issue an approval letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications.

Even if the FDA approves a product, it may limit the approved indications for use of the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including phase 4 clinical trials, be conducted to further assess a drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution and use restrictions or other risk management mechanisms under a REMS which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-marketing studies or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes, and additional labeling claims, are subject to further testing requirements and FDA review and approval.

*Special FDA Expedited Review and Approval Programs*

The FDA has various programs, including fast track designation, accelerated approval and priority review, that are intended to expedite or simplify the process for the development and FDA review of drugs that are intended for the treatment of serious or life threatening diseases or conditions and demonstrate the potential to address unmet medical needs. The purpose of these programs is to provide important new drugs to patients earlier than under standard FDA review procedures.

To be eligible for a fast track designation, the FDA must determine, based on the request of a sponsor, that a product is intended to treat a serious or life threatening disease or condition and demonstrates the potential to address an unmet medical need, or if the drug qualifies as a QIDP under the recently enacted GAIN Act. The FDA will determine that a product will fill an unmet medical need if it will provide a therapy where none exists or provide a therapy that may be potentially superior to existing therapy based on efficacy or safety factors. Fast track designation provides additional opportunities for interaction with the FDA's review team and may allow for rolling review of NDA components before the completed application is submitted. The FDA granted eravacycline fast track designation as a QIDP in April 2014; granted fast track designation and as a QIDP for the IV formulation of TP-271 in September 2015 and for the oral formulation of TP-271 in February 2017. The FDA may decide to rescind the fast track designation if it determines that the qualifying criteria no longer apply.

The FDA may give a priority review designation to drugs that offer major advances in treatment for a serious condition, or provide a treatment where no adequate therapy exists. Most products that are eligible for fast track designation are also likely to be considered appropriate to receive a priority review. A priority review means that the goal for the FDA to review an application is six months, rather than the standard review of ten months under current PDUFA guidelines. Under the new PDUFA agreement, these six and ten month review periods are measured from the "filing" date rather than the receipt date for NDAs for new molecular entities, which typically adds approximately two months to the timeline for review and decision from the date of submission.

In addition, products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may receive accelerated approval, meaning that it may be approved on (1) the basis of adequate and well-controlled clinical trials establishing that the drug product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or (2) on an intermediate clinical endpoint that can be measured earlier than irreversible morbidity or mortality and that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require a sponsor of a drug receiving accelerated approval to perform post-marketing studies to verify and describe the predicted effect on irreversible morbidity or mortality or other clinical endpoint, and the drug may be subject to accelerated withdrawal procedures.

Moreover, under the provisions of the new Food and Drug Administration Safety and Innovation Act, or FDASIA, enacted in 2012, a sponsor can request designation of a product candidate as a "breakthrough therapy." A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Drugs designated as breakthrough therapies are also eligible for accelerated approval. The FDA must take certain actions, such as holding timely meetings and providing advice, intended to expedite the development and review of an application for approval of a breakthrough therapy.

Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

*Post-Approval Requirements*

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing, annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

The FDA may impose a number of post-approval requirements as a condition of approval of an NDA. For example, the FDA may require post-marketing testing, including phase 4 clinical trials, and surveillance to further assess and monitor the product's safety and effectiveness after commercialization.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

The FDA strictly regulates the marketing, labeling, advertising and promotion of drug products that are placed on the market. A product cannot be commercially promoted before it is approved, and approved drugs may generally be promoted only for their approved indications. Promotional claims must also be consistent with the product's FDA-approved label, including claims related to safety and effectiveness. The FDA and other federal agencies also closely regulate the promotion of drugs in specific contexts such as direct-to-consumer advertising, industry-sponsored scientific and education activities, and promotional activities involving the Internet and social media.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market.

Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in mandatory revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences of regulatory non-compliance include, among other things:

- restrictions on, or suspensions of, the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- interruption of production processes, including the shutdown of manufacturing facilities or production lines or the imposition of new manufacturing requirements;
- fines, warning letters or other enforcement letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or PDMA, which regulates the distribution of drugs and drug samples at the federal level, and sets minimum standards for the registration and regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution.

***Exclusivity and Approval of Competing Products***

*Hatch-Waxman Exclusivity*

Market and data exclusivity provisions under the FDCA can delay the submission or the approval of certain applications for competing products. The FDCA provides a five-year period of non-patent data exclusivity within the United States to the first applicant to gain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the activity of the drug substance. We believe that eravacycline and our other product candidates are new chemical entities. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application, or ANDA, or a 505(b)(2) NDA submitted by another company that references the previously approved drug. However, an ANDA or 505(b)(2) NDA may be submitted after four years if it contains a certification of patent invalidity or non-infringement. The FDCA also provides three years of marketing exclusivity for an NDA, 505(b)(2) NDA, or supplement to an existing NDA or 505(b)(2) NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant, are deemed by the FDA to be essential to the approval of the application or supplement. Three year exclusivity may be awarded for changes to a previously approved drug product, such as new indications, dosages, strengths or dosage forms of an existing drug. This three-year exclusivity covers only the conditions of use associated with the new clinical investigations and, as a general matter, does not prohibit the FDA from approving ANDAs or 505(b)(2) NDAs for generic versions of the original, unmodified drug product. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA; however, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness. For drug products that contain an "antibiotic" ingredient approved prior to 1997, such as tetracycline, the statute imposes certain limitations on the award of non-patent exclusivity. However, we do not believe these limitations would apply to eravacycline or any of our other investigational antibiotics.

*Qualified Infectious Disease Product Exclusivity*

Under the GAIN provisions of FDASIA, which was signed into law in July 2012, the FDA may designate a product as a "qualified infectious disease product," or QIDP. In order to receive this designation, a drug must qualify as an antibacterial or antifungal drug for human use intended to treat serious or life-threatening infections, including those caused by either (1) an antibacterial or antifungal resistant pathogen, including novel or emerging infectious pathogens, or (2) a so-called "qualifying pathogen" found on a list of potentially dangerous, drug-resistant organisms to be established and maintained by the FDA under the new law. A sponsor must request such designation before submitting a marketing application. We obtained a QIDP designation for the IV formulation of eravacycline for cUTI and cIAI in July 2013, the oral formulation in March 2014, the IV formulation of TP-271 in September 2015, the oral formulation of TP-271 in February 2017, and expect to request QIDP designations for our other product candidates prior to submitting a marketing application for such product candidates, as appropriate.

Upon approving an application for a qualified infectious disease product, the FDA will extend by an additional five years any non-patent marketing exclusivity period awarded, such as a five-year exclusivity period awarded for a new molecular entity. This extension is in addition to any pediatric exclusivity extension awarded, and the extension will be awarded only to a drug first approved on or after the date of enactment.

The GAIN provisions prohibit the grant of an exclusivity extension where the application is a supplement to an application for which an extension is in effect or has expired, is a subsequent application for a specified change to an approved product, or is an application for a product that does not meet the definition of qualified infectious disease product based on the uses for which it is ultimately approved.

***Foreign Regulation***

In addition to regulations in the United States, we will be subject to a variety of foreign regulations governing clinical trials and commercial sales and distribution of our products. Whether or not we obtain FDA approval for a product, we must obtain approval by the comparable regulatory authorities of foreign countries or economic areas, such as the European Union, before we may commence clinical trials or market products in those countries or areas. The approval process and requirements governing the conduct of clinical trials, product authorization, pricing and reimbursement vary greatly from place to place, and the time may be longer or shorter than that required for FDA approval.

Under European Union regulatory systems, a company may submit marketing authorization applications either under a centralized or decentralized procedure. The centralized procedure is compulsory for medicinal products produced by biotechnology or those medicinal products containing new active substances for specific indications such as the treatment of AIDS, cancer, neurodegenerative disorders, diabetes, viral diseases and designated orphan medicines, and optional for other medicines which are highly innovative. Under the centralized procedure, a marketing application is submitted to the European Medicines Agency where it will be evaluated by the Committee for Medicinal Products for Human Use and a favorable opinion typically results in the grant by the European Commission of a single marketing authorization that is valid for all European Union member states within 67 days of receipt of the opinion. The initial marketing authorization is valid for five years, but once renewed is usually valid for an unlimited period. The decentralized procedure provides for approval by one or more "concerned" member states based on an assessment of an application performed by one member state, known as the "reference" member state. Under the decentralized approval procedure, an applicant submits an application, or dossier, and related materials to the reference member state and concerned member states. The reference member state prepares a draft assessment and drafts of the related materials within 120 days after receipt of a valid application. Within 90 days of receiving the reference member state's assessment report, each concerned member state must decide whether to approve the assessment report and related materials. If a member state does not recognize the marketing authorization, the disputed points are eventually referred to the European Commission, whose decision is binding on all member states.

***Pharmaceutical Coverage and Reimbursement***

Sales of our products will depend, in part, on the availability and extent of coverage and reimbursement by third-party payors, such as government health programs, including Medicare and Medicaid, commercial insurance and managed healthcare organizations. These third-party payors are increasingly challenging the price and limiting the coverage and reimbursement amounts for medical products and services.

The containment of healthcare costs has become a priority of federal and state governments, and the prices of drugs have been a focus in this effort. The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on coverage and reimbursement, and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit our net revenue and results. Decreases in third-party reimbursement for our product candidates or a decision by a third-party payor to not cover our product candidates could reduce physician usage of the product candidate and have a material adverse effect on our sales, results of operations and financial condition.

In the U.S., the federal government provides health insurance for people who are 65 or older, and certain people with disabilities or certain conditions irrespective of their age, through the Medicare program, which is administered by the Centers for Medicare & Medicaid Services, or CMS. Coverage and reimbursement for products and services under Medicare are determined in accordance with the Social Security Act and pursuant to regulations promulgated by CMS, as well as the agency's subregulatory coverage and reimbursement guidance and determinations.

Medicaid is a health insurance program for low-income children, families, pregnant women, and people with disabilities that is jointly funded by the federal and state governments, but administered by the states. In general, state Medicaid programs are required to cover drugs and biologicals of manufacturers that have entered into a Medicaid Drug Rebate Agreement, although such drugs and biologicals may be subject to prior authorization or other utilization controls.

The U.S. Congress and state legislatures from time to time propose and adopt initiatives aimed at cost containment, which could impact our ability to sell our products profitably. Recently, a number of legislative reform measures have been passed to contain healthcare reimbursement for pharmaceuticals, including drugs such as our product candidates. For example, the federal Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, known collectively as ACA, among other things, establishes annual fees to be paid by manufacturers for certain branded prescription drugs, requires manufacturers to participate in a discount program for certain outpatient drugs under Medicare Part D, increases manufacturer rebate liabilities under the Medicaid Drug Rebate Program for outpatient drugs dispensed to Medicaid recipients, addresses a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are line extensions of current drugs, and expands oversight and support for the federal government's comparative effectiveness research of services and products. In addition, other legislative changes have been proposed and adopted since the ACA was enacted. We cannot predict the full impact of ACA or future reform measures on our operations.

In addition, in some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, in the EU, the sole legal instrument at the EU level governing the pricing and reimbursement of medicinal products is Council Directive 89/105/EEC, or the Price Transparency Directive. The aim of this Directive is to ensure that pricing and reimbursement mechanisms established in the EU Member States are transparent and objective, do not hinder the free movement of and trade in medicinal products in the EU, and do not hinder, prevent or distort competition on the market. The Price Transparency Directive does not provide any guidance concerning the specific criteria on the basis of which pricing and reimbursement decisions are to be made in individual EU Member States, nor does it have any direct consequence for pricing or reimbursement levels in individual EU Member States. The EU Member States are free to restrict the range of medicinal products for which their national health insurance systems provide reimbursement, and to control the prices and/or reimbursement levels of medicinal products for human use. An EU Member State may approve a specific price or level of reimbursement for the medicinal product, or alternatively adopt a system of direct or indirect controls on the profitability of the company responsible for placing the medicinal product on the market, including volume-based arrangements, caps and reference pricing mechanisms.

Health Technology Assessment, or HTA, of medicinal products is becoming an increasingly common part of the pricing and reimbursement procedures in some EU Member States, including the United Kingdom, France, Germany, Ireland, Italy and Sweden. The HTA process in the EU Member States is governed by the national laws of these countries. HTA is the procedure according to which the assessment of the public health impact, therapeutic impact, and the economic and societal impact of use of a given medicinal product in the national healthcare systems of the individual country is conducted. HTA generally focuses on the clinical efficacy and effectiveness, safety, cost, and cost-effectiveness of individual medicinal products as well as their potential implications for the healthcare system. Those elements of medicinal products are compared with other treatment options available on the market. The outcome of HTA regarding specific medicinal products will often influence the pricing and reimbursement status granted to these medicinal products by the competent authorities of individual EU Member States. The extent to which pricing and reimbursement decisions are influenced by the HTA of the specific medicinal product vary between EU Member States. A negative HTA of one of our products by a leading and recognized HTA body, such as the National Institute for Health and Care Excellence in the United Kingdom, could not only undermine our ability to obtain reimbursement for such product in the EU Member State in which such negative assessment was issued, but also in other EU Member States. For example, EU Member States that have not yet developed HTA mechanisms could rely to some extent on the HTA performed in countries with a developed HTA framework, such as the United Kingdom, when adopting decisions concerning the pricing and reimbursement of a specific medicinal product.

***Other Healthcare Laws***

Although we currently do not have any products on the market, if our drug candidates are approved and we begin commercialization, we may be subject to additional healthcare regulation and enforcement by the federal government and by authorities in the states and foreign jurisdictions in which we conduct our business. Such laws include, without limitation, state and federal anti-kickback, fraud and abuse, false claims, privacy and security and physician sunshine laws and regulations. If our operations are found to be in violation of any of such laws or any other governmental regulations that apply to us, we may be subject to penalties, including, without limitation, civil and criminal penalties, damages, fines, the curtailment or restructuring of our operations, exclusion from participation in federal and state healthcare programs and imprisonment, any of which could adversely affect our ability to operate our business and our financial results.

**Legal Proceedings**

We are not currently a party to any material legal proceedings.

**Employees**

As of March 5, 2018, we had 78 full-time employees, 50 of whom were primarily engaged in research and development activities. A total of 24 employees have an M.D. or Ph.D. degree. None of our employees is represented by a labor union and we consider our employee relations to be good.

**Available Information**

We file reports and other information with the Securities and Exchange Commission as required by the Securities Exchange Act of 1934, as amended, which we refer to as the Exchange Act. You can find, copy and inspect information we file at the SEC's Public Reference Room, which is located at 100 F Street, N.E., Room 1580, Washington, DC 20549, on official business days during the hours of 10:00 a.m. to 3:00 p.m. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the SEC's Public Reference Room. You can review our electronically filed reports and other information that we file with the SEC on the SEC's web site at http://www.sec.gov.

We were incorporated under the laws of the State of Delaware on July 7, 2006 as Tetraphase Pharmaceuticals, Inc. Our principal executive offices are located at 480 Arsenal Way, Watertown, Massachusetts, 02472, and our telephone number is (617) 715-3600. Our Internet website is http://www.tphase.com. We make available free of charge through our website our Annual Report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to those reports filed or furnished pursuant to Sections 13(a) and 15(d) of the Exchange Act. We make these reports available through our website as soon as reasonably practicable after we electronically file such reports with, or furnish such reports to, the SEC. In addition, we regularly use our website to post information regarding our business, product development programs and governance, and we encourage investors to use our website, particularly the information in the section entitled "Investor Relations," as a source of information about us.

The foregoing references to our website are not intended to, nor shall they be deemed to, incorporate information on our website into this Annual Report on Form 10-K by reference.

**Item 1A. Risk Factors**

Our business faces many risks. We caution you that the following important factors, among others, could cause our actual results to differ materially from those expressed in forward-looking statements made by us or on our behalf in this Annual Report on Form 10-K and other filings with the SEC, press releases, communications with investors and oral statements. The risks described below may not be the only risks we face. Additional risks we do not yet know of or which we currently believe are immaterial may also impair our business operations. If any of the events or circumstances described in the following risks actually occurs, our business, financial condition or results of operations could suffer and the trading price of our common stock could decline.

**Risks Relating to Our Financial Position and Need for Additional Capital**

***We have incurred significant losses since inception, expect to incur losses for at least the next several years and may never achieve or sustain profitability.***

We have incurred annual net operating losses in every year since our inception. Our net loss was $114.8 million for the year ended December 31, 2017, $77.5 million for the year ended December 31, 2016 and $83.2 million for the year ended December 31, 2015. As of December 31, 2017, we had an accumulated deficit of $461.9 million. We have not generated any product revenues and have financed our operations primarily through the public offering and private placements of our equity securities, debt financings and revenue from U.S. government grants and contract awards. We have not completed development of any product candidate and have devoted substantially all of our financial resources and efforts to research and development, including preclinical and clinical development.

We expect to continue to incur significant expenses and operating losses for at least the next several years. The net losses we incur may fluctuate significantly from quarter to quarter. Net losses and negative cash flows have had, and will continue to have, an adverse effect on our stockholders' equity and working capital.

We expect that our expenses will decrease in 2018 compared with 2017, as the completion of the IGNITE clinical program will offset cost increases associated with conducting pre-commercialization activities for eravacycline and, if approved, the launch of eravacycline. If we obtain marketing approval for eravacycline, we do expect to incur significant sales, marketing, distribution and outsourced manufacturing expenses. More specifically, if we obtain marketing approval of eravacycline, we expect to incur significant sales, marketing, and distribution and outsourced manufacturing expenses. Our expenses may increase if and as we:

- maintain, expand and protect our intellectual property portfolio;
- in-license or acquire other products and technologies; and
- add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts.

Our ability to become and remain profitable depends on our ability to generate revenue. We do not expect to generate significant revenue unless and until we obtain marketing approval for, and commercialize, eravacycline, which will require us to be successful in a range of challenging activities, including:

- obtaining marketing approval for eravacycline;
- protecting and maintaining our rights to our intellectual property portfolio related to eravacycline;
- contracting for the manufacture of commercial quantities of eravacycline; and
- establishing sales, marketing and distribution capabilities to effectively market and sell eravacycline.

Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve profitability. Our expenses could increase if we are required by the U.S. Food and Drug Administration, or FDA, or the European Medicines Agency, or EMA, to perform clinical trials and non-clinical studies in addition to those that have been conducted or are currently expected, or if there are any delays in the development of any of our product candidates or the manufacture of any of our product candidates.

We may be unable to develop and commercialize eravacycline or any other product candidate and, even if we do, may never achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, expand our business or continue our operations. A decline in the value of our company could cause our stockholders to lose all or part of their investment in us.

***We expect that we will need additional funding. If we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.***

Developing pharmaceutical products, including conducting preclinical studies, clinical trials and manufacturing activities, is a time-consuming, expensive and uncertain process that takes years to complete. We expect that our expenses will decrease in 2018 compared with 2017, as the completion of the IGNITE clinical program will offset cost increases associated with conducting pre-commercialization activities for eravacycline and, if approved, the launch of eravacycline. If we obtain marketing approval for eravacycline, we do expect to incur significant sales, marketing, distribution and outsourced manufacturing expenses.

We believe that our existing cash and cash equivalents will enable us to fund our operating expenses and capital expenditures, potentially obtain regulatory approvals in the United States and Europe for IV eravacycline for the treatment of complicated intra-abdominal infections, or cIAI, and to perform pre-commercialization activities and commercially launch eravacycline for the treatment of cIAI, if approved. It is also possible that we will not achieve the progress that we expect with respect to eravacycline because the actual costs and timing of regulatory activities are difficult to predict and are subject to substantial risks and delays. As a result, we will be required to obtain further funding through public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources.

These estimates are based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Changing circumstances could cause us to consume capital significantly faster than we currently anticipate, and we may need to spend more money than currently expected because of circumstances beyond our control.

Adequate additional financing may not be available to us on acceptable terms, or at all. Our failure to raise capital as and when needed would have a negative impact on our financial condition and our ability to pursue our business strategy.

Our future funding requirements, both short-term and long-term, will depend on many factors, including:

- the outcome, timing and costs of seeking regulatory approvals generally;
- the costs of commercialization activities for eravacycline and other product candidates if we receive marketing approval, including the timing and costs of establishing product sales, marketing, distribution and manufacturing capabilities;
- the timing and costs of manufacturing activities in anticipation of commercial launch of eravacycline;
- the timing and costs of our ongoing clinical trials for our product candidates;
- the amount of funding that we receive under our subcontracts awarded to us by our collaborator CUBRC, Inc., or CUBRC, under its government contracts with the Biomedical Advanced Research and Development Authority, or BARDA, and with the National Institutes of Health's, or NIH's, National Institute of Allergy and Infectious Diseases, or NIAID, and under our subaward from CUBRC under its grant from NIAID, and our award from the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator, or CARB-X, and the activities funded under these contracts;
- the number and characteristics of product candidates that we pursue;
- the timing and costs of developing eravacycline for additional indications;
- revenue received from commercial sales of eravacycline, subject to receipt of marketing approval;
- the terms and timing of any future collaborations, partnerships, licensing, marketing, distribution or other arrangements that we may establish;
- the amount and timing of any payments we may be required to make, or that we may receive, in connection with the licensing, filing, prosecution, defense and enforcement of any patents or other intellectual property rights, including milestone and royalty payments and patent prosecution fees that we are obligated to pay to Harvard pursuant to our license agreement;
- the costs of maintaining and protecting our intellectual property rights and defending against intellectual property related claims; and
- the extent to which we in-license or acquire other products and technologies.

***Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.***

Currently, our only external source of funds is funding under subcontracts awarded to us by CUBRC pursuant to government contracts from BARDA and NIAID, and an award from CARB-X. Although the BARDA contract and our subcontract with CUBRC under the BARDA contract have terms which currently expire on September 30, 2018, BARDA is entitled to terminate the project for convenience at any time, and is not obligated to provide continued funding beyond current-year amounts from congressionally approved annual appropriations. To the extent that BARDA ceases to provide funding of the program to CUBRC, CUBRC has the right to cease providing funding to us. Committed funding from CUBRC under our BARDA subcontract is for up to $41.9 million from the initial contract date through September 30, 2018, of which $35.7 million had been received through December 31, 2017.

Similarly, although the NIAID contract and our subcontract with CUBRC under the NIAID contract have terms which currently expire on March 31, 2019, NIAID is entitled to terminate the project for convenience at any time, and is not obligated to provide continued funding beyond March 31, 2019. To the extent NIAID ceases to provide funding of the programs to CUBRC, CUBRC has the right to cease providing funding to us. Committed funding from CUBRC under our subcontract with respect to the NIAID contract is for up to $16.9 million, of which $13.2 million had been received through December 31, 2017.

Similarly, although the CARB-X Award has a term which currently expires on December 31, 2018, CARB-X is entitled to terminate the project for convenience at any time. Committed funding from the CARB-X Award is for up to $4.0 million from the initial award date through December 31, 2018, of which $44,000 had been received through December 31, 2017.

As a result, unless and until we can generate a substantial amount of revenue from our product candidates, we expect to finance our future cash needs through public or private equity offerings, debt financings or collaborations and licensing arrangements. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans.

To the extent that we raise additional capital through the sale of common stock, convertible securities or other equity securities, the ownership interest of our stockholders may be materially diluted, and the terms of these securities could include liquidation or other preferences and anti-dilution protections that could adversely affect their rights. In addition, debt financing, if available, would result in increased fixed payment obligations and may involve agreements that include restrictive covenants that limit our ability to take specific corporate actions, such as incurring additional debt, merging with or acquiring another entity, making capital expenditures or declaring dividends, that could adversely impact our ability to conduct our business. In addition, securing additional financing would require a substantial amount of time and attention from our management and may divert a disproportionate amount of their attention away from day-to-day activities, which may adversely affect our management's ability to oversee the development of our product candidates.

If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams or product candidates or to grant licenses on terms that may not be favorable to us.

***We have a limited operating history and no history of commercializing pharmaceutical products, which may make it difficult to evaluate the prospects for our future viability.***

We began operations in the third quarter of 2006. Our operations to date have been limited to financing and staffing our company, developing our technology and developing eravacycline and other product candidates. We have not yet demonstrated an ability to obtain marketing approval, manufacture a commercial scale product, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Consequently, predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully developing and commercializing pharmaceutical products.

**Risks Related to Product Development and Commercialization**

***We are dependent on the success of our lead product candidate, eravacycline, and our ability to develop, obtain marketing approval for and successfully commercialize eravacycline. If we are unable to develop, obtain marketing approval for and successfully commercialize eravacycline or experience significant delays in doing so, our business could be materially harmed.***

We currently have no products approved for sale and have invested a significant portion of our efforts and financial resources in the development of eravacycline for use as a first-line empiric monotherapy for the treatment of multidrug-resistant infections. Specifically, we were developing eravacyline for the treatment of both cIAI and cUTI. We have conducted four phase 3 clinical trials – IGNITE1 and IGNITE4 for the treatment of cIAI and IGNITE2 and IGNITE3 for the treatment of cUTI. We submitted an NDA to the FDA for IV eravacycline for the treatment of cIAI and a marketing authorization application, or MAA, to the EMA for IV eravacycline for the treatment of cIAI. In February 2018, we announced top-line data from IGNITE3, our phase 3 clinical trial evaluating the safety and efficacy of eravacycline with IV administration for the treatment of cUTI. IGNITE3 failed to meet the co-primary efficacy endpoints. As a result, we are no longer developing eravacycline for the treatment of cUTI.

Our prospects are substantially dependent on our ability to develop, obtain marketing approval for and successfully commercialize eravacycline for the treatment of cIAI. The success of eravacycline will depend on several factors, including the following:

- successful outcome of discussions with regulatory agencies regarding our planned marketing applications;
- receipt of marketing approvals from applicable regulatory authorities;
- establishment of arrangements with third-party manufacturers to obtain manufacturing supply;
- obtainment and maintenance of patent and trade secret protection and regulatory exclusivity;
- protection of our rights in our intellectual property portfolio;
- successful manufacturing of commercial scale batches of eravacycline;
- commercial launch of eravacycline, if and when approved, whether alone or in collaboration with others;
- acceptance of eravacycline, if and when approved, by patients, the medical community and third-party payors;
- favorable results of any additional clinical trials involving eravacycline that we may conduct;
- competition with other therapies; and
- a continued acceptable safety profile of eravacycline following approval.

If we are unable to develop, receive marketing approval for, or successfully commercialize eravacycline for the treatment of cIAI, or experience delays as a result of any of these matters or otherwise, our business could be materially harmed.

***If clinical trials of eravacycline or of any other product candidate that we advance to clinical trials fail to demonstrate safety and efficacy to the satisfaction of the FDA or comparable foreign regulatory authorities or do not otherwise produce favorable results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of eravacycline or any other product candidate.***

We are not permitted to commercialize, market, promote, or sell any product candidate in the United States without obtaining marketing approval from the FDA or in other countries without obtaining approvals from comparable foreign regulatory authorities, such as the EMA, and we may never receive such approvals. We must complete extensive preclinical development and clinical trials to demonstrate the safety and efficacy of our product candidates in humans before we will be able to obtain these approvals. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is inherently uncertain as to outcome. We have not previously submitted an NDA to the FDA, an MAA to the EMA or similar drug approval filings to comparable foreign regulatory authorities for any of our product candidates.

The clinical development of eravacycline and other product candidates is susceptible to the risk of failure inherent at any stage of drug development, including failure to achieve efficacy in a trial or across a broad population of patients, the occurrence of severe adverse events, failure to comply with protocols or applicable regulatory requirements, and determination by the FDA or any comparable foreign regulatory authority that a drug product is not approvable. The outcome of preclinical studies and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. For example, although eravacycline achieved favorable results in the lead-in part of IGNITE2, the pivotal portion of IGNITE2 did not meet the primary endpoint of statistical non-inferiority compared to levofloxacin. In July 2017 we announced positive top line data from IGNITE4. Further, in the first quarter of 2018 we reported top-line data for our IGNITE3 phase 3 clinical trial evaluating the safety and efficacy of eravacycline with IV administration for the treatment of cUTI. IGNITE3 failed to meet the co-primary efficacy endpoints of responder rate (a combination of clinical cure and microbiological success) in the microbiological intent-to-treat population at the end-of-IV treatment visit and at the test-of-cure visit, which were evaluated using a 10% non-inferiority margin. We may fail to achieve success in any other future clinical trial of any other product candidate.

In addition, preclinical and clinical data are often susceptible to varying interpretations and analyses. Many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval for the product candidates. Even if we believe that the results of our clinical trials warrant marketing approval, the FDA or comparable foreign regulatory authorities may disagree and may not grant marketing approval of our product candidates.

In some instances, there can be significant variability in safety and/or efficacy results between different trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, adherence to the dosing regimen and other trial protocols and the rate of dropout among clinical trial participants. In addition, in the case of our clinical trials, results may differ on the basis of the type of bacteria with which patients are infected. We cannot be certain that other clinical trials that we may conduct will demonstrate consistent or adequate efficacy and safety to obtain regulatory approval to market our product candidates.

We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent us from obtaining regulatory approval for eravacycline or any of our other product candidates, including:

- clinical trials of our product candidates may produce unfavorable or inconclusive results;
- we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate;
- our third-party contractors, including those manufacturing our product candidates or conducting clinical trials on our behalf, may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- regulators or institutional review boards may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;

- we may have to suspend or terminate clinical trials of our product candidates for various reasons, including a finding that the participants are being exposed to unacceptable health risks, undesirable side effects or other unexpected characteristics of the product candidate;
- regulators or institutional review boards may require that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks, undesirable side effects or other unexpected characteristics of the product candidate;
- the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we enter into agreement for clinical and commercial supplies;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

If we are required to conduct additional clinical trials or other testing of eravacycline, or any other product candidate that we develop beyond the trials and testing that we contemplate, if we are unable to successfully complete clinical trials of our product candidates or other testing, if the results of these trials or tests are unfavorable or are only modestly favorable or if there are safety concerns associated with eravacycline or our other product candidates, we may:

- be delayed in obtaining marketing approval for our product candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or significant safety warnings, including boxed warnings;
- be subject to additional post-marketing testing or other requirements; or
- remove the product from the market after obtaining marketing approval.

Our product development costs will also increase if we experience delays in testing or marketing approvals and we may be required to obtain additional funds to complete clinical trials. We cannot be certain that our clinical trials will begin as planned or be completed on schedule, if at all, or that we will not need to restructure our trials after they have begun. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our product candidates, which may harm our business and results of operations. In addition, many of the factors that cause, or lead to, clinical trial delays may ultimately lead to the denial of regulatory approval of eravacycline or any other product candidate.

***If we experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.***

We may not be able to initiate or continue clinical trials for any other product candidate that we develop if we are unable to locate and enroll a sufficient number of eligible patients to participate in clinical trials for such other product candidate as required by the FDA or comparable foreign regulatory authorities, such as the EMA. Patient enrollment is a significant factor in the timing of clinical trials, and is affected by many factors, including:

- the size and nature of the patient population;
- the severity of the disease under investigation;
- the proximity of patients to clinical sites;
- the eligibility criteria for the trial;
- the design of the clinical trial; and
- competing clinical trials and clinicians' and patients' perceptions as to the potential advantages and risks of the drug being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating.

***Serious adverse events or undesirable side effects or other unexpected properties of eravacycline or any other product candidate may be identified during development or after approval, if obtained, that could delay, prevent or cause the withdrawal of the product candidates' regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if obtained.***

Serious adverse events or undesirable side effects caused by, or other unexpected properties of, our product candidates could cause us, an institutional review board, or regulatory authorities to interrupt, delay or halt our clinical trials and could result in a more restrictive label, the imposition of distribution or use restrictions or the delay or denial of regulatory approval by the FDA or comparable foreign regulatory authorities. If eravacycline or any of our other product candidates are associated with serious adverse events or undesirable side effects or have properties that are unexpected, we may need to abandon their development or limit development to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Many compounds that initially showed promise in clinical or earlier stage testing have later been found to cause undesirable or unexpected side effects that prevented further development of the compound. In our clinical trials of eravacycline, some treatment-related adverse events have been reported. The most common treatment-related adverse events observed in clinical trials of eravacycline have been nausea and emesis. Additional adverse events, undesirable side effects or other unexpected properties of eravacycline or any of our other product candidates could arise or become known either during clinical development or, if approved, after the approved product has been marketed. If such an event occurs during development, our trials could be suspended or terminated and the FDA or comparable foreign regulatory authorities could order us to cease further development of, or deny approval of, eravacycline or our other product candidates. If such an event occurs after eravacycline or such other product candidates are approved, a number of potentially significant negative consequences may result, including:

- regulatory authorities may withdraw the approval of such product;
- regulatory authorities may require additional warnings on the label or impose distribution or use restrictions;
- regulatory authorities may require one or more postmarketing studies;
- we may be required to create a medication guide outlining the risks of such side effects for distribution to patients;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the affected product candidate, if approved, or could substantially increase commercialization costs and expenses, which could delay or prevent us from generating revenues from the sale of our products and harm our business and results of operations.

***Even if eravacycline or any other product candidate that we develop receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success and the market opportunity for eravacycline or other product candidates may be smaller than we estimate.***

We have never commercialized a product candidate for any indication. Even if eravacycline or any other product candidates that we develop are approved by the appropriate regulatory authorities for marketing and sale, they may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. Efforts to educate the medical community and third-party payors on the benefits of our product candidates may require significant resources and may not be successful. If physicians, rightly or wrongly, associate our product candidates with antibiotic resistance issues of other products of the same class, physicians might not prescribe our product candidates for treating a broad range of infections. If eravacycline or any other product candidate that we develop does not achieve an adequate level of market acceptance, we may not generate significant product revenues and, therefore, we may not become profitable. The degree of market acceptance of eravacycline, if approved, or any other product candidate that is approved for commercial sale, will depend on a number of factors, including, but not limited to:

- the efficacy and safety of the product;
- the potential advantages of the product compared to alternative treatments;
- the prevalence and severity of any side effects;
- the clinical indications for which the product is approved;
- limitations or warnings, including distribution or use restrictions, contained in the product's approved labeling or an approved risk evaluation and mitigation strategy;
- our ability to offer the product for sale at competitive prices;

- the product's convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try, and of physicians to prescribe, the product;
- whether the product is designated under physician treatment guidelines as a first-line therapy or as a second- or third-line therapy for particular infections;
- the strength of marketing and distribution support;
- the approval of other new products for the same indications;
- the timing of market introduction of our approved products as well as competitive products;
- the cost of treatment in relation to alternative treatments;
- availability and level of coverage and amount of reimbursement from government payors, managed care plans and other third-party payors;
- the effectiveness of our sales and marketing efforts;
- adverse publicity about the product or favorable publicity about competitive products; and
- the development of resistance by bacterial strains to the product.

In addition, the potential market opportunity for eravacycline is difficult to estimate. Our estimates of the potential market opportunity are predicated on several key assumptions such as industry knowledge, third-party research reports and other surveys. While we believe that our internal assumptions are reasonable, these assumptions involve the exercise of significant judgment on the part of our management, are inherently uncertain and the reasonableness of these assumptions has not been assessed by an independent source. If any of the assumptions proves to be inaccurate, then the actual market for eravacycline could be smaller than our estimates of the potential market opportunity. If the actual market for eravacycline is smaller than we expect, or if the product fails to achieve an adequate level of acceptance by physicians, health care payors and patients, our product revenue may be limited and it may be more difficult for us to achieve or maintain profitability.

***If we are unable to establish sales, marketing and distribution capabilities or enter into sales, marketing and distribution agreements with third parties, we may not be successful in commercializing eravacycline or such other product candidates that we develop if and when eravacycline or any other product candidates are approved.***

We currently do not have a sales, marketing or distribution infrastructure and as a company have little experience in the sales, marketing, or distribution of pharmaceutical products. To achieve commercial success for any approved product, we must either develop a sales and marketing organization or outsource these functions to third parties. We intend to develop and build a commercial organization in the United States and recruit experienced sales, marketing and distribution professionals, which will require substantial resources, will be time-consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing and distribution capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization costs. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel. In addition, we may not be able to hire a sales force in the United States that is sufficient in size or has adequate expertise in the medical markets we intend to target. If we are unable to establish a sales force and marketing and distribution capabilities, our operating results may be adversely affected.

Factors that may inhibit our efforts to commercialize our products on our own include:

- our inability to recruit and retain adequate numbers of effective sales and marketing personnel;
- the ability of sales personnel to obtain access to or persuade adequate numbers of physicians to prescribe any future products;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

We plan to commercialize eravacycline outside the United States with the assistance of collaborators. As a result of entering into arrangements with third parties to perform sales, marketing and distribution services, our product revenues or the profitability of these product revenues to us may be lower than if we were to directly market and sell products in those markets. As an example, if Everest Medicines is unsuccessful in developing eravacycline in the Chinese market, we may not receive any future milestone or royalty payments. Furthermore, we may be unsuccessful in entering into the necessary arrangements with third parties or may be unable to do so on terms that are favorable to us. In addition, we likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively.

If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates.

***We face substantial competition from other pharmaceutical and biotechnology companies and our operating results may suffer if we fail to compete effectively.***

The development and commercialization of new drug products is highly competitive. We face competition from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide with respect to eravacycline and our other product candidates that we may seek to develop or commercialize in the future. There are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of product candidates for the treatment of multidrug-resistant infections. Potential competitors also include academic institutions, government agencies and other public and private research organizations. Our competitors may succeed in developing, acquiring or licensing technologies and drug products that are more effective or less costly than any product candidates that we are currently developing or that we may develop, which could render our product candidates obsolete or noncompetitive.

There are a variety of available therapies marketed for the treatment of resistant or even multidrug-resistant infections that we would expect would compete with eravacycline, including meropenem/vaborbactam, which is being marketed by Melinta Therapeutics as Vabomere, ceftazidime/avibactam, which is marketed by Allergan, Inc. as Avycaz; meropenem, which is marketed by AstraZeneca as Merrem; ceftolozane/tazobactam, imipenem/cilastatin, and ertapenem which are marketed by Merck & Co., Inc. as Zerbaxa, Primaxin and Invanz, respectively; tigecycline, which is marketed by Pfizer, Inc. as Tygacil; and piperacillin/tazobactam, which is marketed by Pfizer, Inc. as Zosyn. Many of the available therapies are well established and widely accepted by physicians, patients and third-party payors. Insurers and other third-party payors may also encourage the use of generic products. If eravacycline is approved, it may be priced at a significant premium over other competitive products. This may make it difficult for eravacycline to compete with these products.

There are also a number of products currently in phase 3 development by third parties to treat multidrug-resistant infections, including plazomicin, which is being developed by Achaogen, Inc., imipenem/relebactam, which is being developed by Merck & Co., Inc., and cefiderocol, which is being developed by Shionogi. Some of these companies may obtain marketing approval from the FDA or comparable foreign regulatory authorities for their product candidates more rapidly than we do, which could result in our competitors establishing a strong market position before we are able to enter the market.

Many of our competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials and obtaining regulatory approvals than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and other early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

In July 2012, the Food and Drug Administration Safety and Innovation Act was passed, which included the GAIN Act. The GAIN Act is intended to provide incentives for the development of new, qualified infectious disease products. These incentives may result in more competition in the market for new antibiotics, and may cause pharmaceutical and biotechnology companies with more resources than we have to shift their efforts towards the development of products that could be competitive with eravacycline and our other product candidates.

***Even if we are able to commercialize eravacycline or any other product candidate that we develop, the product may become subject to unfavorable pricing regulations, third-party payor coverage and reimbursement policies or healthcare reform initiatives that could harm our business.***

Marketing approvals, pricing, coverage and reimbursement for new drug products vary widely from country to country. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, which may negatively impact the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain marketing approval.

Our ability to commercialize eravacycline or any other product candidate will depend in part on the extent to which coverage and reimbursement for these products and related treatments will be available from government authorities, private health insurers, health maintenance organizations and other third-party payors. The healthcare industry is acutely focused on cost containment, both in the United States and elsewhere. As a result, government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications, which could affect our ability to sell our product candidates profitably.

There may also be delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the indications for which the drug is approved by the FDA or comparable foreign regulatory authorities. Increasingly, third-party payors are requiring higher levels of evidence of the benefits and clinical outcomes of new technologies and are challenging the prices charged. Moreover, obtaining coverage does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Reimbursement rates may vary, by way of example, according to the use of the drug and the clinical setting in which it is used. Reimbursement rates may also be based in part on existing reimbursement amounts for lower cost drugs or may be bundled into the payments for other services.

We cannot be sure that coverage will be available for eravacycline or any other product candidate that we commercialize and, if available, that the reimbursement rates will be adequate. Further, the net reimbursement for drug products may be subject to additional reductions if there are changes to laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. An inability to promptly obtain coverage and adequate payment rates from both government-funded and private payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

***Product liability lawsuits against us could divert our resources, cause us to incur substantial liabilities and limit commercialization of any products that we may develop.***

We face an inherent risk of product liability claims as a result of the clinical testing of our product candidates despite obtaining appropriate informed consents from our clinical trial participants. We will face an even greater risk if we commercially sell eravacycline or any other product candidate that we develop. For example, we may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during clinical testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability or a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Regardless of the merits or eventual outcome, liability claims may result in:

- reduced resources of our management to pursue our business strategy;
- decreased demand for our product candidates or products that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- initiation of investigations by regulators;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- significant costs to defend resulting litigation;
- substantial monetary awards to trial participants or patients;

- loss of revenue; and
- the inability to commercialize any products that we may develop.

Although we maintain general liability insurance of $6 million in the aggregate and clinical trial liability insurance of $6 million in the aggregate for all product candidates, this insurance may not fully cover potential liabilities that we may incur. The cost of any product liability litigation or other proceeding, even if resolved in our favor, could be substantial. We will need to increase our insurance coverage if and when we begin selling eravacycline or any other product candidate that receives marketing approval. In addition, insurance coverage is becoming increasingly expensive. If we are unable to obtain or maintain sufficient insurance coverage at an acceptable cost or to otherwise protect against potential product liability claims, it could prevent or inhibit the development and commercial production and sale of our product candidates, which could adversely affect our business, financial condition, results of operations and prospects.

***If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on our business.***

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. From time to time and in the future, our operations may involve the use of hazardous and flammable materials, including chemicals and biological materials, and may also produce hazardous waste products. Even if we contract with third parties for the disposal of these materials and wastes, we cannot completely eliminate the risk of contamination or injury resulting from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

We maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, but this insurance may not provide adequate coverage against potential liabilities. However, we do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. Current or future environmental laws and regulations may impair our research, development or production efforts, which could adversely affect our business, financial condition, results of operations or prospects. In addition, failure to comply with these laws and regulations may result in substantial fines, penalties or other sanctions.

***Our research and development efforts may not result in additional drug candidates being discovered on anticipated timelines, which could limit our ability to generate revenues.***

Some of our research and development programs are at preclinical stages. Additional drug candidates that we may develop or acquire will require significant commitment of resources. We cannot predict whether our research will lead to the discovery and development of any additional drug candidates that could generate revenues for us.

**Risks Related to Our Dependence on Third Parties**

***We expect to depend on collaborations with third parties for the development and commercialization of some of our product candidates. Our prospects with respect to those product candidates will depend in part on the success of those collaborations.***

Although we expect to commercialize eravacycline ourselves in the United States, we intend to seek to commercialize eravacycline outside the United States through collaboration arrangements. For instance, in February 2018, we entered into a license agreement with Everest Medicines Limited whereby we granted Everest Medicines an exclusive license to develop and commercialize eravacycline for the treatment of complicated intra-abdominal infections and other indications, in mainland China and several other Asian territories and countries. In addition, we may seek third-party collaborators for development and commercialization of other product candidates. Our likely collaborators for any marketing, distribution, development, licensing or broader collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. We are not currently party to any such arrangements.

We may derive revenue from research and development fees, license fees, milestone payments and royalties under any collaborative arrangement into which we enter. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements. In addition, our collaborators

may have the right to abandon research or development projects and terminate applicable agreements, including funding obligations, prior to or upon the expiration of the agreed upon terms. As a result, we can expect to relinquish some or all of the control over the future success of a product candidate that we license to a third party.

Collaborations involving our product candidates, such as our license arrangement with Everest Medicines, may pose a number of risks, including the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected or in compliance with applicable regulatory requirements;
- collaborators may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the commercialization of our product candidates;
- a collaborator with marketing and distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of such product or products;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;
- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability; and
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates.

Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If a collaborator of ours is involved in a business combination, it could decide to delay, diminish or terminate the development or commercialization of any product candidate licensed to it by us.

***We may have to alter our development and commercialization plans if we are not able to establish collaborations.***

We will require additional funds to complete the development and potential commercialization of eravacycline and our other product candidates. For some of our product candidates, we may decide to collaborate with pharmaceutical and biotechnology companies for the development and potential commercialization of those product candidates. For example, we intend to utilize a variety of types of collaboration arrangements for commercialization of eravacycline outside the United States. Our ability to enter into any such collaboration may be significantly delayed, or the terms on which we enter into collaborations may be adversely affected, due to the unfavorable results of IGNITE3.

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include:

- the design or results of clinical trials, such as the negative results of our clinical trials of eravacycline for the treatment of cUTI;
- the likelihood of approval by the FDA or comparable foreign regulatory authorities;

- the potential market for the subject product candidate;
- the costs and complexities of manufacturing and delivering such product candidate to patients;
- the potential for competing products;
- our patent position protecting the product candidate, including any uncertainty with respect to our ownership of our technology or our licensor's ownership of technology we license from them, which can exist if there is a challenge to such ownership without regard to the merits of the challenge;
- the need to seek licenses or sub-licenses to third-party intellectual property; and
- industry and market conditions generally.

The collaborator may also consider alternative product candidates or technologies for similar indications that may be available for collaboration and whether such collaboration could be more attractive than the one with us for our product candidate. We may also be restricted under future license agreements from entering into agreements on certain terms with potential collaborators. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

If we are unable to reach agreements with suitable collaborators on a timely basis, on acceptable terms, or at all, we may have to curtail the development of a product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to fund and undertake development or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms or at all. If we fail to enter into collaborations and do not have sufficient funds or expertise to undertake the necessary development and commercialization activities, we may not be able to further develop our product candidates or bring them to market and our business may be materially and adversely affected.

***We rely on third parties to conduct our clinical trials. If they do not perform satisfactorily, our business may be materially harmed.***

We do not independently conduct clinical trials of eravacycline. We rely on third parties, such as contract research organizations, clinical data management organizations, medical institutions and clinical investigators, to conduct our clinical trials. Any of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements, it would delay our product development activities.

Our reliance on these third parties for clinical development activities limits our control over these activities but we remain responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards. For example, notwithstanding the obligations of a contract research organization for a trial of one of our product candidates, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with standards, commonly referred to as current Good Clinical Practices, or cGCPs, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. The FDA enforces these cGCPs through periodic inspections of trial sponsors, principal investigators, clinical trial sites and institutional review boards. If we or our third-party contractors fail to comply with applicable cGCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA may require us to perform additional clinical trials before approving our product candidates, which would delay the regulatory approval process. We cannot be certain that, upon inspection, the FDA will determine that any of our clinical trials comply with cGCPs. We are also required to register clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

Furthermore, the third parties conducting clinical trials on our behalf are not our employees, and except for remedies available to us under our agreements with such contractors, we cannot control whether or not they devote sufficient time and resources to our ongoing development programs. These contractors may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug development activities, which could impede their ability to devote appropriate time to our clinical programs. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we may not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates. If that occurs, we will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates. In such an event, our financial results and the commercial prospects for eravacycline or any other product candidates that we seek to develop could be harmed, our costs could increase and our ability to generate revenues could be delayed, impaired or foreclosed.

We also rely on other third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing approval of our product candidates or commercialization of any resulting products, producing additional losses and depriving us of potential product revenue.

***We contract with third parties for the manufacture of eravacycline for clinical trials and expect to continue to do so in connection with the commercialization of eravacycline and for clinical trials and commercialization of any other product candidates that we develop. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.***

We do not currently have nor do we plan to build the internal infrastructure or capability to manufacture eravacycline or our other product candidates for use in the conduct of our clinical trials or for commercial supply. We currently rely on and expect to continue to rely on third-party contract manufacturers to manufacture clinical supplies of eravacycline and our other product candidates, and we have relied and expect to continue to rely on third-party contract manufacturers to manufacture registration batches and commercial quantities of any product candidate that we commercialize following approval for marketing by applicable regulatory authorities. Reliance on third-party manufacturers entails risks, including:

- delays in the manufacture of our clinical drug supply, registration and validation batches and commercial supply if our third-party manufacturers give greater priority to the supply of other products over our product candidates or otherwise do not satisfactorily perform according to the terms of the agreement between us;
- equipment malfunctions, power outages or other general disruptions experienced by our third-party manufacturers to their respective operations and other general problems with a multi-step manufacturing process;
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us;
- the possible breach of the manufacturing agreement by the third-party;
- the failure of the third-party manufacturer to comply with applicable regulatory requirements; and
- the possible misappropriation of our proprietary information, including our trade secrets and know-how.

We currently rely on a small number of third-party contract manufacturers for all of our required raw materials, drug substance and finished product for our preclinical research and clinical trials. We do not have long-term agreements with any of these third parties. We also do not have any current contractual relationships for the manufacture of commercial supplies of any of our other product candidates. If any of our existing manufacturers should become unavailable to us for any reason, we may incur some delay in identifying or qualifying replacements.

If any of our product candidates are approved by any regulatory agency, we intend to enter into agreements with third-party contract manufacturers for the commercial production of those products. This process is difficult and time consuming and we may face competition for access to manufacturing facilities as there are a limited number of contract manufacturers operating under cGMPs that are capable of manufacturing our product candidates. Consequently, we may not be able to reach agreement with third-party manufacturers on satisfactory terms, which could delay our commercialization.

Third-party manufacturers are required to comply with cGMPs and similar regulatory requirements outside the United States. Facilities used by our third-party manufacturers must be inspected by the FDA after we submit an NDA and before potential approval of the product candidate. Similar regulations apply to manufacturers of our product candidates for use or sale in foreign countries. We do not control the manufacturing process and are completely dependent on our third-party manufacturers for compliance with the applicable regulatory requirements for the manufacture of our product candidates. If our manufacturers cannot successfully manufacture material that conforms to the strict regulatory requirements of the FDA and any applicable foreign regulatory authority, they will not be able to secure the applicable approval for their manufacturing facilities. If these facilities are not approved for commercial manufacture, we may need to find alternative manufacturing facilities, which could result in delays in obtaining approval for the applicable product candidate as alternative qualified manufacturing facilities may not be available on a timely basis or at all. In addition, our manufacturers are subject to ongoing periodic unannounced inspections by the FDA and corresponding state and foreign agencies for compliance with cGMPs and similar regulatory requirements. Failure by any of our manufacturers to comply with applicable cGMPs or other regulatory requirements could result in sanctions being imposed on us or the contract manufacturer, including fines, injunctions, civil penalties, delays, suspensions or withdrawals of approvals, operating restrictions, interruptions in supply and criminal prosecutions, any of which could significantly and adversely affect supplies of our product candidates and have a material adverse impact on our business, financial condition and results of operations.

Our current and anticipated future dependence upon others for the manufacture of eravacycline and any other product candidate that we develop may adversely affect our future profit margins and our ability to commercialize any products that receive marketing approval on a timely and competitive basis.

***If we fail to comply with our obligations in the agreements under which we in-license or acquire development or commercialization rights to products or technology from third parties, we could lose commercial rights that are important to our business.***

We are a party to a license agreement with Harvard that imposes, and we may enter into additional agreements, including license agreements, with other parties in the future that impose, diligence, development and commercialization timelines, milestone payment, royalty, insurance and other obligations on us. For instance, under our license agreement with Harvard, we are obligated to satisfy diligence requirements, including using commercially reasonable efforts to develop and commercialize licensed compounds and to implement a specified development plan, meeting specified development milestones and providing an update on progress on an annual basis. If we fail to comply with these obligations, our counterparties may have the right to terminate these agreements, in which event we might not be able to develop, manufacture or market any product that is covered by these agreements, which could materially adversely affect the value of the product candidate being developed under any such agreement. Termination of these agreements or reduction or elimination of our rights under these agreements may result in our having to negotiate new or reinstated agreements with less favorable terms, or cause us to lose our rights under these agreements, including our rights to important intellectual property or technology.

**Risks Related to Our Intellectual Property**

***If we are unable to obtain and maintain sufficient patent protection for our technology or our product candidates, or if the scope of the patent protection is not sufficiently broad, our competitors could develop and commercialize technology and products similar or identical to ours, and our ability to successfully commercialize our technology and product candidates may be adversely affected.***

Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our proprietary chemistry technology and product candidates. If we do not adequately protect our intellectual property, competitors may be able to use our technologies and erode or negate any competitive advantage we may have, which could harm our business and ability to achieve profitability. To protect our proprietary position, we file patent applications in the United States and abroad related to our novel technologies and product candidates that are important to our business. The patent application and approval process is expensive and time consuming. We may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. We may also fail to identify patentable aspects of our research and development before it is too late to obtain patent protection.

Under our license agreement with Harvard, Harvard retains the right to prosecute and maintain specified Harvard patents and patent applications in the field of tetracycline chemistry, which are exclusively licensed to us under the agreement. Moreover, if we license technology or product candidates from third parties in the future, those licensors may retain the right to prosecute, maintain and enforce the patent rights that they license to us with or without our involvement. Because control of prosecution and maintenance rests with Harvard, and prosecution, maintenance and enforcement could rest with future licensors, we cannot be certain that these in-licensed patents and applications will be prosecuted, maintained and enforced in a manner consistent with the best interests of our business. If Harvard fails to prosecute or maintain, or future licensors fail to prosecute, maintain or enforce, those patents necessary for any of our product candidates, our ability to develop and commercialize those product candidates may be adversely affected and we may not be able to prevent competitors from making and selling competing products.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain. No consistent policy regarding the breadth of claims allowed in biotechnology and pharmaceutical patents has emerged to date in the United States or in many foreign jurisdictions. In addition, the determination of patent rights with respect to pharmaceutical compounds and technologies commonly involves complex legal and factual questions, which has in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Furthermore, recent changes in patent laws in the United States, including the America Invents Act of 2011, may affect the scope, strength and enforceability of our patent rights or the nature of proceedings which may be brought by us related to our patent rights.

Our pending and future patent applications may not result in patents being issued that protect our technology or product candidates, in whole or in part, or that effectively prevent others from commercializing competitive technologies and products. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection.

As a result of the America Invents Act of 2011, the United States transitioned to a first-inventor-to-file system in March 2013, under which, assuming the other requirements for patentability are met, the first inventor to file a patent application is entitled to the patent. However, as a result of the lag in the publication of patent applications following filing in the United States, we are not able to be certain upon filing that we are the first to file for patent protection for any invention. Moreover, we may be subject to a third-party preissuance submission of prior art to the U.S. Patent and Trademark Office, or become involved in opposition, derivation, reexamination, *inter partes* review or interference proceedings, in the United States or elsewhere, challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of or invalidate our patent rights, allow third parties to commercialize our technology or product candidates and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights.

Even if our patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our owned or licensed patents by developing similar or alternative technologies or products in a non-infringing manner. Our competitors may seek to market generic versions of any approved products by submitting Abbreviated New Drug Applications to the FDA in which they claim that patents owned or licensed by us are invalid, unenforceable and/or not infringed. Alternatively, our competitors may seek approval to market their own products similar to or otherwise competitive with our products. In these circumstances, we may need to defend and/or assert our patents, including by filing lawsuits alleging patent infringement. In any of these types of proceedings, a court or other agency with jurisdiction may find our patents invalid and/or unenforceable. Even if we have valid and enforceable patents, these patents still may not provide protection against competing products or processes sufficient to achieve our business objectives.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. In addition, given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized.

***We may become involved in lawsuits to protect or enforce our patents or other intellectual property, which could be expensive, time consuming and unsuccessful.***

Competitors may infringe our patents, trademarks, copyrights or other intellectual property, or those of our licensors. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming and divert the time and attention of our management and scientific personnel. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents. In addition, in a patent infringement proceeding, there is a risk that a court will decide that a patent of ours is invalid or unenforceable, in whole or in part, and that we do not have the right to stop the other party from using the invention at issue. There is also a risk that, even if the validity of such patents is upheld, the court will construe the patent's claims narrowly or decide that we do not have the right to stop the other party from using the invention at issue on the grounds that our patents do not cover the invention. An adverse outcome in a litigation or proceeding involving our patents could limit our ability to assert our patents against those parties or other competitors, and may curtail or preclude our ability to exclude third parties from making and selling similar or competitive products. Any of these occurrences could adversely affect our competitive business position, business prospects and financial condition. Similarly, if we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable, or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of such trademarks.

In any infringement litigation, any award of monetary damages we receive may not be commercially valuable. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during litigation. Moreover, there can be no assurance that we will have sufficient financial or other resources to file and pursue such infringement claims, which typically last for years before they are concluded. Even if we ultimately prevail in such claims, the monetary cost of such litigation and the diversion of the attention of our management and scientific personnel could outweigh any benefit we receive as a result of the proceedings.

***If we are sued for infringing intellectual property rights of third parties, such litigation could be costly and time consuming and could prevent or delay us from developing or commercializing our product candidates.***

Our commercial success depends, in part, on our ability to develop, manufacture, market and sell our product candidates and use our proprietary chemistry technology without infringing the intellectual property and other proprietary rights of third parties. Numerous third-party U.S. and non-U.S. issued patents and pending applications exist in the area of antibacterial treatment, including compounds, formulations, treatment methods and synthetic processes that may be applied towards the synthesis of antibiotics. If any of their patents or patent applications cover our product candidates or technologies, we may not be free to manufacture or market our product candidates as planned. We are aware of a third-party U.S. patent claiming pharmaceutical compositions of tetracyclines. The third-party U.S. patent could be asserted against us with respect to eravacycline. We believe we have defenses in the event that the third party seeks to assert such patent against us, including the invalidity of the relevant claims of such patent. However, we may not be successful in asserting these defenses, including proving invalidity, and could be found to infringe the third party's patent, which would have a material adverse effect on us.

There is a substantial amount of intellectual property litigation in the biotechnology and pharmaceutical industries, and we may become party to, or threatened with, litigation or other adversarial proceedings regarding intellectual property rights with respect to our technology or product candidates, including patent infringement litigation with respect to the third-party U.S. patent referred to above, and eravacycline. Other possible adversarial proceedings include interference proceedings before the U.S. Patent and Trademark Office. Third parties may assert infringement claims against us based on existing or future intellectual property rights. The outcome of intellectual property litigation is subject to uncertainties that cannot be adequately quantified in advance. The pharmaceutical and biotechnology industries have produced a significant number of patents, and it may not always be clear to industry participants, including us, which patents cover various types of products or methods of use. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform. If we are sued for patent infringement, we would need to demonstrate that our product candidates, products or methods either do not infringe the patent claims of the relevant patent or that the patent claims are invalid, and we may not be able to do this. Proving invalidity is difficult. For example, in the United States, proving invalidity requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents. Even if we are successful in these proceedings, we may incur substantial costs and the time and attention of our management and scientific personnel could be diverted in pursuing these proceedings, which could have a material adverse effect on us. In addition, we may not have sufficient resources to bring these actions to a successful conclusion.

If we are found to infringe a third-party's intellectual property rights, such as the third-party U.S. patent referred to above, we could be ordered by a court, to cease developing, manufacturing, using, selling or offering for sale the infringing product. Alternatively, we may conclude that we need to obtain a license from such third-party in order to use the infringing technology and continue developing, manufacturing or marketing the infringing product or product candidate. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

***We may be subject to claims that we or our employees have misappropriated the intellectual property of a third-party, or claiming ownership of what we regard as our own intellectual property.***

Many of our employees were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees do not use the intellectual property and other proprietary information or know-how of others in their work for us, we may be subject to claims that we or these employees have used or disclosed such intellectual property or other proprietary information. Litigation may be necessary to defend against these claims.

In addition, while we typically require our employees, consultants and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own. Moreover, because we have licensed intellectual property from Harvard, we must rely on Harvard's practices with regard to the assignment of intellectual property to it. To the extent we or Harvard have failed to obtain such assignments or such assignments are breached, we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property. If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to our management and scientific personnel.

***If we are unable to protect the confidentiality of our trade secrets, the value of our technology could be materially adversely affected and our business would be harmed.***

In addition to seeking patents for some of our technology and products, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, in seeking to develop and maintain a competitive position. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our consultants, independent contractors, advisors, corporate collaborators, outside scientific collaborators, contract manufacturers, suppliers and other third parties. We, as well as our licensors, also enter into confidentiality and invention or patent assignment agreements with employees and certain consultants. Any party with whom we or Harvard have executed such an agreement may breach that agreement and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, if any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent such third-party, or those to whom they communicate such technology or information, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our business and competitive position could be harmed.

***We have not yet completed registration of our trademarks. Failure to secure those registrations could adversely affect our business.***

Four trademark applications for TETRAPHASE PHARMACEUTICALS, our logo, and combinations of those have been allowed in the United States, meaning that we can perfect our registrations when we have commenced use in commerce. TETRAPHASE PHARMACEUTICALS is registered in nine other jurisdictions and pending in three others. If we do not secure registrations for our trademarks, we may encounter more difficulty in enforcing them against third parties than we otherwise would, which could adversely affect our business. We own pending trademark applications for two proposed proprietary names for the eravacycline product in the United States, but they have not yet been examined and could be rejected and opposed, and registrations for the proposed proprietary product names may not be obtained, maintained or enforced. We do not yet own applications to register the proprietary product name outside the United States and the availability of the proposed names for registration and use in foreign jurisdictions is not known. In addition, in the United States Patent and Trademark Office and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to seek to cancel registered trademarks. Cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings. We have also obtained registration for our design work in two jurisdictions, and applications remain pending for those design marks in the United States and one other jurisdiction.

In addition, any proprietary name we propose to use with eravacycline or any other product candidate in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. The FDA typically conducts a review of proposed product names, including an evaluation of potential for confusion with other product names. If the FDA objects to any of our proposed proprietary product names, we may be required to expend significant additional resources in an effort to identify a suitable proprietary product name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA.

**Risks Related to Regulatory Approval and Other Legal Compliance Matters**

***If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize eravacycline or any other product candidate that we develop, and our ability to generate revenue will be materially impaired.***

Our product candidates, including eravacycline, and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, marketing, export, sale and distribution, are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by comparable foreign regulatory authorities, with regulations differing from country to country. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate. We currently do not have any products approved for sale in any jurisdiction. We have only limited experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third-party contract research organizations to assist us in this process.

We are not permitted to market our product candidates in the United States until we receive approval of an NDA from the FDA. We have not submitted an NDA for any of our product candidates. An NDA must include extensive preclinical and clinical data and supporting information to establish the product candidate's safety and efficacy for each desired indication. The NDA must also include significant information regarding the chemistry, manufacturing and controls for the product candidate. Obtaining approval of an NDA is a lengthy, expensive and uncertain process. The FDA review process typically takes years to complete. The FDA has substantial discretion in the approval process and may refuse to accept for filing any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies or additional information regarding chemistry, manufacturing and controls for the product candidate. Foreign regulatory authorities have differing requirements for approval of drug candidates with which we must comply prior to marketing. Obtaining marketing approval for marketing of a product candidate in one country does not ensure that we will be able to obtain marketing approval in other countries, but the failure to obtain marketing approval in one jurisdiction could negatively impact our ability to obtain marketing approval in other jurisdictions. Delays in approvals or rejections of marketing applications in the United States or foreign countries may be based upon many factors, including regulatory requests for additional analyses, reports, data and studies, regulatory questions regarding, or different interpretations of, data and results, changes in regulatory policy during the period of product development and the emergence of new information regarding product candidates or related products. The FDA or equivalent foreign regulatory authorities may determine that eravacycline or any other product candidate that we develop is not effective, or is only moderately effective, or has undesirable or unintended side effects, toxicities, safety profile or other characteristics that preclude marketing approval or prevent or limit commercial use. The FDA may also find during its pre-approval inspection that the facilities identified in our NDA fail to comply with cGMP requirements, thereby delaying or preventing approval. In addition, any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable. If we experience delays in obtaining approval or if we fail to obtain approval of eravacycline or any other product candidate that we develop, the commercial prospects for eravacycline or such other product candidate may be harmed and our ability to generate revenues will be materially impaired.

***A fast track designation by the FDA does not guarantee approval and may not actually lead to a faster development, regulatory review or approval process.***

If a product is intended for the treatment of a serious or life-threatening condition and the product demonstrates the potential to address unmet medical needs for that condition, the treatment sponsor may apply for FDA fast track designation. The FDA granted eravacycline fast track designation as a qualified infectious disease product in April 2014, granted fast track designation as a qualified infectious disease product for the IV formulation of TP-271 in September 2015, and granted fast track designation as a qualified infectious disease product for the oral formulation of TP-271 in February 2017. Fast track designation does not ensure approval or a faster development, regulatory review or approval process compared to conventional FDA procedures. Additionally, the FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program.

***If we are unable to obtain marketing approval in international jurisdictions, we will not be able to market our product candidates abroad.***

In order to market and sell eravacycline and any other product candidate that we develop in the European Union and many other jurisdictions, we must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. The approval procedure varies among countries and can involve additional testing. In addition, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We may not obtain approvals from regulatory authorities outside the United States on a timely basis or at all.

Additionally, on June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the European Union, commonly referred to as Brexit. On March 29, 2017, the country formally notified the European Union of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty. Since a significant proportion of the regulatory framework in the United Kingdom is derived from European Union directives and regulations, the referendum could materially impact the regulatory regime with respect to the approval of our product candidates in the United Kingdom or the European Union. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, would prevent us from commercializing our product candidates in the United Kingdom and/or the European Union and restrict our ability to generate revenue and achieve and sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the United Kingdom and/or European Union for our product candidates, which could significantly and materially harm our business.

***If we receive regulatory approval for any product candidates, including eravacycline, we will be subject to ongoing obligations and continuing regulatory review, which may result in significant additional expense. Our product candidates, including eravacycline, if approved, could be subject to restrictions or withdrawal from the market, and we may be subject to penalties, if we fail to comply with regulatory requirements or if we experience unanticipated problems with our product candidates, when and if approved.***

Any product candidate, including eravacycline, for which we obtain marketing approval, will also be subject to ongoing regulatory requirements for labeling, manufacturing, packaging, storage, distribution, advertising, promotion, record-keeping and submission of safety and other post-market information. For example, approved products, manufacturers and manufacturers' facilities are required to comply with extensive FDA requirements, including ensuring that quality control and manufacturing procedures conform to cGMPs. As such, we and our contract manufacturers will be subject to continual review and periodic inspections to assess compliance with cGMPs. Accordingly, we and others with whom we work must continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production and quality control. We will also be required to report certain adverse reactions and production problems, if any, to the FDA and to comply with requirements concerning advertising and promotion for our products.

In addition, even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed, may be subject to significant conditions of approval or may impose requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the product. The FDA closely regulates the post-approval marketing and promotion of drugs to ensure drugs are marketed only for the approved indications and in accordance with the provisions of the approved labeling and regulatory requirements. The FDA also imposes stringent restrictions on manufacturers' communications regarding off-label use and if we do not restrict the marketing of our products only to their approved indications, we may be subject to enforcement action for off-label marketing.

If a regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, or disagrees with the promotion, marketing or labeling of a product, it may impose restrictions on that product or us. In addition, if any product fails to comply with applicable regulatory requirements, a regulatory agency may:

- issue warning or untitled letters;
- mandate modifications to promotional materials or require provision of corrective information to healthcare practitioners and patients;
- impose restrictions on the product or its manufacturers or manufacturing processes;
- impose restrictions on the labeling or marketing of the product;
- impose restrictions on product distribution or use;
- require post-marketing clinical trials;
- require withdrawal of the product from the market;
- refuse to approve pending applications or supplements to approved applications that we submit;
- require recall of the product;
- require entry into a consent decree, which can include imposition of various fines (including restitution or disgorgement of profits or revenue), reimbursements for inspection costs, required due dates for specific actions and penalties for noncompliance;
- suspend, vary, modify or withdraw marketing approvals;
- refuse to permit the import or export of the product;
- seize or detain supplies of the product; or
- issue injunctions, levy fines or impose other civil and/or criminal penalties.

***Our relationships with customers and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.***

Our future arrangements with third-party payors, healthcare professionals and customers who purchase, recommend or prescribe our product candidates will be subject to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute any products for which we obtain marketing approval. These laws and regulations include, for example, the false claims and anti-kickback statutes and regulations. At such time as we market, sell and distribute any products for which we obtain marketing approval, it is possible that our business activities could be subject to challenge under one or more of these laws and regulations. Restrictions under applicable federal and state healthcare laws and regulations include the following:

- the federal Anti-Kickback Statute, among other things, prohibits persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under federally funded healthcare programs such as Medicare and Medicaid;
- the federal False Claims Act imposes criminal and civil penalties, which can be enforced by private citizens through civil whistleblower and qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program and creates federal criminal laws that prohibit knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services;
- the federal transparency requirements under the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively, the ACA, requires manufacturers of covered drugs, devices, biologics and medical supplies to report to the Department of Health and Human Services information related to payments and other transfers of value to physicians and teaching hospitals and physician ownership and investment interests; and
- analogous state laws and regulations, such as state anti-kickback and false claims laws that may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers; state laws that require pharmaceutical companies to implement compliance programs, comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government or track and report gifts, compensation and other remuneration provided to physicians and other health care providers; and state and foreign laws that govern the privacy and security of health information in specified circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, which complicates compliance efforts.

We will be required to spend substantial time and money to ensure that our business arrangements with third parties comply with applicable healthcare laws and regulations. Even then, governmental authorities may conclude that our business practices do not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. Recent healthcare reform legislation has strengthened these federal and state healthcare laws. For example, the ACA amends the intent requirement of the federal anti-kickback and criminal healthcare fraud statutes. A person or entity no longer needs to have actual knowledge of these statutes or a specific intent to violate them. In addition, the ACA provides that the government may assert that a claim that includes items or services resulting from a violation of the federal anti-kickback statute constitutes a false or fraudulent claim for purposes of the False Claims Act. If governmental authorities find that our operations violate any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and we may be required to curtail or restructure our operations. Moreover, we expect that there will continue to be federal and state laws and regulations, proposed and implemented, that could impact our operations and business. The extent to which future legislation or regulations, if any, relating to healthcare fraud and abuse laws or enforcement, may be enacted or what effect such legislation or regulation would have on our business remains uncertain.

***If we successfully commercialize one of our drug candidates, failure to comply with our reporting and payment obligations under U.S. governmental pricing programs could have a material adverse effect on our business, financial condition and results of operations.***

If we participate in the Medicaid Drug Rebate Program once we successfully commercialize a drug, we will be required to report certain pricing information for our products to the Centers for Medicare & Medicaid Services, the federal agency that administers the Medicaid and Medicare programs. We may also be required to report pricing information to the Department of Veterans Affairs. If we become subject to these reporting requirements, we will be liable for errors associated with our submission of pricing data, for failure to report pricing data in a timely manner, and for overcharging government payers, which can result in civil monetary penalties under the Medicaid statute, the federal civil False Claims Act, and other laws and regulations.

***Recently enacted and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and affect the prices we may obtain.***

Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and expanding access to healthcare. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. We expect to experience pricing pressures in connection with the sale of any products that we develop, due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative proposals.

In March 2010, the ACA became law in the United States with the goals of broadening access to health insurance, reducing or constraining the growth of healthcare spending, enhancing remedies against fraud and abuse, adding new transparency requirements for health care and health insurance industries and imposing additional health policy reforms. Further, the new law includes annual fees to be paid by manufacturers for certain branded prescription drugs, requires manufacturers to participate in a discount program for certain outpatient drugs under Medicare Part D, increases manufacturer rebate responsibilities under the Medicaid Drug Rebate Program for outpatient drugs dispensed to Medicaid recipients, addresses a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for line extensions and for drugs that are inhaled, infused, instilled, implanted or injected and expands oversight and support for the federal government's comparative effectiveness research of services and products.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. On August 2, 2011, the Budget Control Act of 2011 created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of up to 2% per fiscal year, which went into effect on April 1, 2013. On January 2, 2013, President Obama signed into law the American Taxpayer Relief Act of 2012 which reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by the United States Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

**Risks Related to Employee Matters and Managing Growth**

***Our future success depends on our ability to retain our chief executive officer and other key executives and to attract, retain and motivate qualified personnel.***

Our industry has experienced a high rate of turnover of management personnel in recent years. We are highly dependent on the development, regulatory, commercialization and business development expertise of our executive management team, as well as the other principal members of our management, scientific and clinical team. Although we have formal employment agreements with our executive officers, these agreements do not prevent them from terminating their employment with us at any time. For instance, in December 2017, our former chief medical officer terminated his employment with us.

We do not have formal employment agreements with any of our other employees. If we lose one or more of our executive officers or key employees, our ability to implement our business strategy successfully could be seriously harmed. We may face difficulty attracting and retaining our executive officers and key employees as a consequence of the results of IGNITE3. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to develop, gain regulatory approval of and commercialize products successfully. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these additional key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to develop and commercialize drug candidates will be limited.

***We expect to grow our organization, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.***

We expect to experience growth in the number of our employees and the scope of our operations, particularly in the areas of drug development, regulatory affairs and sales, marketing and distribution. Our management may need to divert a disproportionate amount of its attention away from our day-to-day activities to devote time to managing these growth activities. To manage these growth activities, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. Our inability to effectively manage the expansion of our operations may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Our expected growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of additional product candidates. If our management is unable to effectively manage our expected growth, our expenses may increase more than expected, our ability to generate revenues could be reduced and we may not be able to implement our business strategy.

***The business that we conduct outside the United States may be adversely affected by international risk and uncertainties.***

Although our operations are based in the United States, we conduct business outside the United States and expect to continue to do so in the future. For instance, many of the sites at which our clinical trials are or may be conducted are outside the United States. In addition, we plan to seek approvals to sell our products in foreign countries. Any business that we conduct outside the United States will be subject to additional risks that may materially adversely affect our ability to conduct business in international markets, including:

- potentially reduced protection for intellectual property rights;
- the potential for so-called parallel importing, which is what happens when a local seller, faced with high or higher local prices, opts to import goods from a foreign market (with low or lower prices) rather than buying them locally;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- production shortages resulting from any events affecting a product candidate and/or finished drug product supply or manufacturing capabilities abroad;
- business interruptions resulting from geo-political actions, including war and terrorism, or natural disasters, including earthquakes, hurricanes, typhoons, floods and fires; and
- failure to comply with Office of Foreign Asset Control rules and regulations and the Foreign Corrupt Practices Act.

***Our internal computer systems, or those of any collaborators, contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product development programs or overall business operations.***

Our internal computer infrastructure and those of any collaborators, contractors or consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. While we have not experienced any such material system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability, our competitive position could be harmed and the further development and commercialization of our product candidates could be delayed or halted.

**Risks Related to Our Common Stock**

***The price of our common stock may be volatile and fluctuate substantially, which could result in substantial losses for purchasers of our common stock.***

Our stock price may be volatile. The stock market in general and the market for smaller pharmaceutical and biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. For example, our stock traded within a range of a high price of $52.90 per share and a low price of $2.05 per share for the period beginning March 20, 2013, our first day of trading on the NASDAQ Global Select Market, through March 1, 2018. As a result of this volatility, investors may not be able to sell their common stock at or above the prices they paid for it. The market price for our common stock may be influenced by many factors, including:

- the filing and approval of marketing applications;
- the timing of clinical trials of our product candidates;
- results of clinical trials of our product candidates;
- regulatory actions by the FDA or equivalent authorities in foreign jurisdictions with respect to eravacycline and any other product candidate;
- failure or discontinuation of any of our development programs;
- the success of existing or new competitive products or technologies;
- results of clinical trials of product candidates of our competitors;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our product candidates or clinical development programs;
- the results of our efforts to develop, in-license or acquire additional product candidates or products;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- announcement or expectation of additional financing efforts;
- sales of our common stock by us, our insiders or other stockholders;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in estimates or recommendations by securities analysts, if any, that cover our stock;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;

- general economic, industry and market conditions; and
- the other factors described in this "Risk Factors" section.

***We have been and may again be subject to class action litigation and have been subject to shareholder derivative litigation due to stock price volatility, which could distract our management and could result in substantial costs or large judgments against us.***

The stock market frequently experiences extreme price and volume fluctuations. We have experienced significant declines in our stock price following our announcements that our phase 3 clinical trials for eravacycline for the treatment of patients with cUTI did not meet the primary endpoint of those trials. In addition, the market prices of securities of companies in the biotechnology and pharmaceutical industry have been extremely volatile and have experienced fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. These fluctuations could adversely affect the market price of our common stock. In the past, securities class action litigation has often been brought against companies following periods of volatility in the market prices of their securities. In fact, in January 2016 and March 2016, two class action lawsuits were filed against us, our chief executive officer and certain former executives in the United States District Court for the District of Massachusetts. These cases were subsequently consolidated. In November 2017 plaintiffs withdrew a pending appeal in the United States Court of Appeals for the First Circuit. In addition, in May 2016, a shareholder derivative action was filed against our chief executive officer, certain former executive officers, all the members of our current board of directors, a former board member, and against us as nominal defendant, in Massachusetts Superior Court (Suffolk County). This case was subsequently dismissed by the court without prejudice due to the plaintiff's failure to properly perfect service of process. Due to the volatility in our stock price, we may be the target of similar litigation in the future.

We may be the subject of future litigation, including as a result of our announcement of the failure of IGNITE3 to meet its co-primary endpoints. In connection with any such future litigation, we could incur substantial costs and such costs and any related settlements or judgments may not be covered by insurance. We could also suffer an adverse impact on our reputation and a diversion of management's attention and resources, which could cause serious harm to our business, operating results and financial condition.

***An active trading market for our common stock may not be sustained.***

Although we have listed our common stock on The NASDAQ Global Select Market, an active trading market for our common stock may not be sustained. In the absence of an active trading market for our common stock, investors may not be able to sell their common stock at or above the price at which they acquired the common stock or at the times that they would like to sell. An inactive trading market may also impair our ability to raise capital to continue to fund operations by selling shares and may impair our ability to acquire other companies or technologies by using our shares as consideration.

***If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, our share price and trading volume could decline.***

The trading market for our common stock will depend on the research and reports that securities or industry analysts publish about us or our business. We do not have any control over these analysts. There can be no assurance that analysts will cover us, or provide favorable coverage. If one or more analysts downgrade our stock or change their opinion of our stock, our share price would likely decline. In addition, if one or more analysts cease coverage of our company or fail to regularly publish reports on us, we could lose visibility in the financial markets, which could cause our share price or trading volume to decline.

***We have broad discretion in the use of our cash reserves and may not use them effectively.***

Our management has broad discretion to use our cash reserves and could spend these reserves in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses that could have a material adverse effect on our business, cause the price of our common stock to decline and delay the development of our product candidates. Pending their use, we may invest our cash reserves in a manner that does not produce income or that loses value.

***We have incurred increased costs as a result of operating as a public company, and our management is required to devote substantial time to new compliance initiatives and corporate governance practices.***

As a public company we incur significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The NASDAQ Global Select Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have increased our legal and financial compliance costs and have made some activities more time-consuming and costly especially since we are no longer an "emerging growth company", as defined in the Jumpstart Our Business Startups Act of 2012, and are no longer able to take advantage of certain exemptions from various reporting requirements that are applicable to public companies that are "emerging growth companies" and that were applicable to us prior to January 1, 2016.

***Failure to maintain effective internal controls in accordance with Section 404 of the Sarbanes-Oxley Act in the future could have a material adverse effect on our ability to produce accurate financial statements and on our stock price.***

Section 404 of the Sarbanes-Oxley Act of 2002 requires us, on an annual basis, to review and evaluate our internal controls. To maintain compliance with Section 404, we are required to document and evaluate our internal control over financial reporting, which has been both costly and challenging. We will need to continue to dedicate internal resources, continue to engage outside consultants and follow a detailed work plan to continue to assess and document the adequacy of internal control over financial reporting, continue to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. There is a risk that in the future neither we nor our independent registered public accounting firm will be able to conclude within the prescribed timeframe that our internal control over financial reporting is effective as required by Section 404. If we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

***We do not anticipate paying any cash dividends on our capital stock in the foreseeable future; accordingly, stockholders must rely on capital appreciation, if any, for any return on their investment.***

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the operation, development and growth of our business. The terms of our term loan facility with Silicon Valley Bank and Oxford Finance that we repaid precluded us from paying dividends, and any future debt agreements may also preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be the sole source of gain for our stockholders for the foreseeable future.

***Provisions in our corporate charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.***

Provisions in our corporate charter and our by-laws may discourage, delay or prevent a merger, acquisition or other change in control of us that stockholders may consider favorable, including transactions in which our stockholders might otherwise receive a premium for their shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

- establish a classified board of directors such that all members of the board are not elected at one time;
- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- limit the manner in which stockholders can remove directors from the board;
- establish advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted on at stockholder meetings;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call a special meeting of stockholder meetings;

- authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a "poison pill" that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and
- require the approval of the holders of at least 75% of the votes that all our stockholders would be entitled to cast to amend or repeal certain provisions of our charter or by-laws.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner. This could discourage, delay or prevent someone from acquiring us or merging with us, whether or not it is desired by, or beneficial to, our stockholders.

**ITEM 1B. Unresolved Staff Comments**

None.

**ITEM 2. Properties**

We lease our principal facilities, which consist of approximately 37,438 square feet of office, research and laboratory space located at 480 Arsenal Way, Watertown, Massachusetts. The leases covering this space expire on November 30, 2019. We believe that our existing facilities are sufficient for our current needs. In the third quarter of 2016, we entered into a sublease with respect to a portion of our principal facilities with an unrelated third party. The term of the sublease expires in November 2019.

**ITEM 3. Legal Proceedings**

In January 2016 and March 2016, two securities class action lawsuits were filed against us, our chief executive officer, our former chief operating officer and our former chief financial officer, in the United States District Court for the District of Massachusetts. In May 2016, the court consolidated the two lawsuits and appointed lead plaintiffs and lead counsel. The lead plaintiffs filed a consolidated amended complaint in July 2016 and filed a second consolidated amended complaint in August 2016. The second amended complaint was brought on behalf of an alleged class of those who purchased our common stock between March 5, 2015 and September 8, 2015, and alleged claims arising under Sections 10 and 20 of the Exchange Act of 2934, as amended. The complaint generally alleged that the defendants violated the federal securities laws by, among other things, making material misstatements or omissions concerning IGNITE2. The complaint sought, among other relief, unspecified compensatory damages, attorneys' fees and costs. In October 2016, we filed a motion to dismiss the second amended complaint in its entirety, which plaintiffs opposed. Our motion to dismiss was granted by the United States District Court for the District of Massachusetts in May 2017. In July 2017 plaintiffs appealed this decision to the United States Court of Appeals for the First Circuit, or the First Circuit. In November 2017 plaintiffs withdrew their appeal to the First Circuit.

**ITEM 4. Mine Safety Disclosures**

Not applicable.

## PART II

### ITEM 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

***Market Price Information***

Our common stock began trading on the NASDAQ Global Select Market on March 20, 2013 under the symbol "TTPH". Prior to that date, there was no established public trading market for our common stock. The following table sets forth, for the periods indicated, the high and low intraday sales prices of our common stock as reported by the NASDAQ Global Select Market:

| | High | Low |
|---|---|---|
| **2017** | | |
| First Quarter | $ 9.93 | $ 3.57 |
| Second Quarter | $ 9.53 | $ 6.41 |
| Third Quarter | $ 8.75 | $ 5.28 |
| Fourth Quarter | $ 7.98 | $ 5.60 |

| | High | Low |
|---|---|---|
| **2016** | | |
| First Quarter | $ 9.98 | $ 3.48 |
| Second Quarter | $ 6.28 | $ 3.12 |
| Third Quarter | $ 4.65 | $ 3.62 |
| Fourth Quarter | $ 5.12 | $ 3.11 |

***Holders***

At March 5, 2018, there were approximately 8 holders of record of our common stock. We believe that the number of beneficial owners of our common stock at that date was substantially greater.

***Dividends***

We have never declared or paid any cash dividends on our common stock. We currently intend to retain earnings, if any, for use in our business and do not anticipate paying cash dividends on our common stock in the foreseeable future. Payment of future dividends, if any, on our common stock will be at the discretion of our board of directors after taking into account various factors, including our financial condition, operating results, anticipated cash needs, and plans for expansion.

***Securities Authorized for Issuance under Equity Compensation Plans***

The information required by this item will be set forth in the definitive proxy statement we will file in connection with our 2018 Annual Meeting of Stockholders and is incorporated by reference herein.

***Purchase of Equity Securities***

We did not purchase any of our equity securities during the period covered by this Annual Report on Form 10-K.

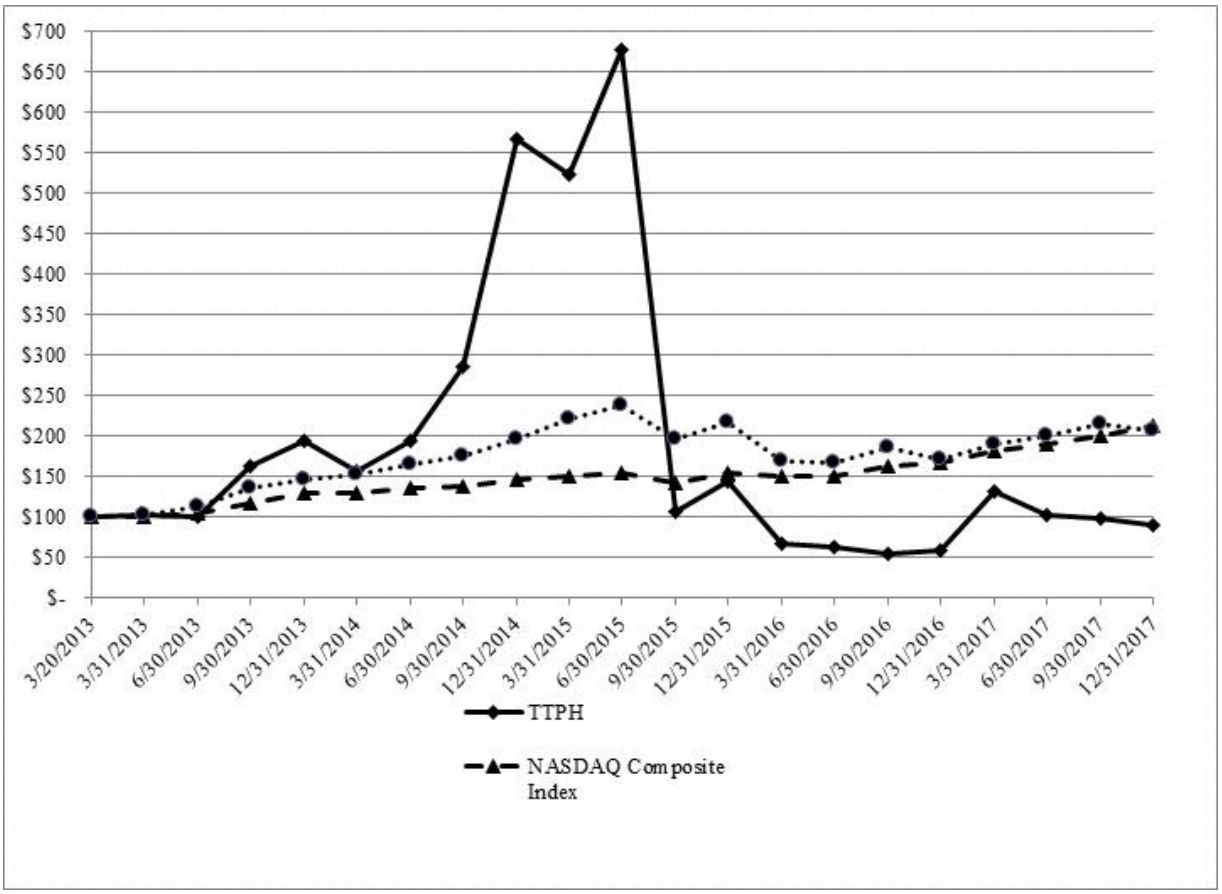
***Unregistered Sales of Equity Securities***

We did not issue any unregistered securities during the period covered by this Annual Report on Form 10-K.

***Comparative Stock Performance Graph***

The information included under the heading "Comparative Stock Performance Graph" in this Item 5 of Part II of this Annual Report on Form 10-K shall not be deemed to be "soliciting material" or subject to Regulation 14A or 14C, shall not be deemed "filed" for purposes of Section 18 of the Exchange Act, or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act.

Set forth below is a graph comparing the total cumulative returns of Tetraphase, the NASDAQ Composite Index and the NASDAQ Biotechnology Index. The graph assumes $100 was invested on March 20, 2013 in our common stock and each of the indices and that all dividends, if any, are reinvested.




| | 3/20/13 | 12/31/13 | 12/31/14 | 12/31/15 | 12/31/16 | 12/31/17 |
|---|---|---|---|---|---|---|
| Tetraphase Pharmaceuticals | $ 100.00 | $ 193.14 | $ 567.29 | $ 143.29 | $ 57.57 | $ 90.00 |
| NASDAQ Composite Index | $ 100.00 | $ 128.34 | $ 145.54 | $ 153.88 | $ 165.42 | $ 212.14 |
| NASDAQ Biotechnology Index | $ 100.00 | $ 145.52 | $ 195.14 | $ 217.43 | $ 170.28 | $ 206.14 |

**ITEM 6. Selected Financial Data**

The following selected consolidated financial data should be read in conjunction with our Consolidated Financial Statements and the Notes thereto and Management's Discussion and Analysis of Financial Condition and Results of Operations included elsewhere in this Annual Report on Form 10-K. The selected consolidated financial data in this section are not intended to replace our financial statements and the related notes. Our historical results are not necessarily indicative of the results that may be expected in the future.

The consolidated statement of operations data for each of the three years in the period ended December 31, 2017 and the consolidated balance sheet data at December 31, 2017 and 2016 have been derived from our audited consolidated financial statements for such years, included elsewhere in this Annual Report on Form 10-K. The statement of operations data for the years ended December 31, 2014 and 2013 and the consolidated balance sheet data at December 31, 2015, 2014 and 2013 have been derived from the audited consolidated financial statements for such years not included in this Annual Report on Form 10-K.

Our historical results for any prior period are not necessarily indicative of results to be expected in any future period.

| | Year Ended December 31, | | | | |
|---|---|---|---|---|---|
| | 2017 | 2016 | 2015 | 2014 | 2013 |
| | (in thousands, except per share data) | | | | |
| **Statement of Operations data:** | | | | | |
| Contract and grant revenue | $ 9,666 | $ 5,145 | $ 11,686 | $ 9,098 | $ 10,486 |
| Operating expenses: | | | | | |
| Research and development | 101,706 | 63,764 | 73,768 | 61,932 | 31,508 |
| General and administrative | 23,675 | 19,211 | 20,916 | 12,932 | 7,168 |
| Total operating expenses | 125,381 | 82,975 | 94,684 | 74,864 | 38,676 |
| Loss from operations | (115,715) | (77,830) | (82,998) | (65,766) | (28,190) |
| Other income (expense): | | | | | |
| Other income (expense) | 963 | 350 | (191) | (976) | (1,446) |
| Total other income (expense) | 963 | 350 | (191) | (976) | (1,446) |
| Net loss | $ (114,752) | $ (77,480) | $ (83,189) | $ (66,742) | $ (29,636) |
| Net loss per share-basic and diluted | $ (2.63) | $ (2.11) | $ (2.36) | $ (2.49) | $ (1.78) |
| Weighted-average number of common shares used in net loss per share-basic and diluted | 43,582 | 36,704 | 35,261 | 26,807 | 16,665 |

| | As of December 31, | | | | |
|---|---|---|---|---|---|
| | 2017 | 2016 | 2015 | 2014 | 2013 |
| | (in thousands) | | | | |
| **Balance Sheet Data:** | | | | | |
| Cash and cash equivalents | $ 136,411 | $ 142,086 | $ 205,912 | $ 121,042 | $ 102,712 |
| Working capital | 128,921 | 138,962 | 203,071 | 109,321 | 92,229 |
| Total assets | 149,040 | 151,710 | 214,917 | 127,204 | 105,886 |
| Current liabilities | 18,525 | 11,495 | 10,697 | 17,276 | 13,191 |
| Long-term obligations | 105 | 162 | 165 | 1,362 | 4,887 |
| Accumulated deficit | (461,884) | (347,132) | (269,652) | (186,463) | (119,721) |
| Total stockholders' equity | $ 130,410 | $ 140,053 | $ 204,055 | $ 108,566 | $ 87,808 |

## ITEM 7. Management's Discussion and Analysis of Financial Condition and Results of Operations

*You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and related notes appearing in this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10-K, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the "Risk Factors" section of this Annual Report on Form 10-K, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.*

### Overview

We are a clinical-stage biopharmaceutical company using our proprietary chemistry technology to create novel antibiotics for serious and life-threatening multidrug-resistant infections. We are developing our lead product candidate, eravacycline, a fully synthetic fluorocycline, as an intravenous, or IV antibiotic for use as a first-line empiric monotherapy for the treatment of multidrug-resistant infections, including multidrug-resistant, or MDR, Gram-negative infections in patients, such as those with complicated intra-abdominal infections, or cIAI.

We conducted a global phase 3 clinical program for eravacycline called IGNITE (**I**nvestigating **G**ram-**N**egative **I**nfections **T**reated with **E**ravacycline).

On July 25, 2017, we announced top-line data from our IGNITE4 trial, a global phase 3 randomized, double-blind, double-dummy, multicenter, prospective study assessing the efficacy, safety and pharmacokinetics of twice-daily intravenous, or IV, eravacycline (1.0 mg/kg every 12 hours) compared with meropenem (1g every 8 hours) for the treatment of complicated intra-abdominal infections, or cIAI that we conducted in 500 patients. In the trial, eravacycline met the primary endpoint of statistical non-inferiority of clinical response at the test-of-cure, or TOC, visit, under the guidance set by the United States Food and Drug Administration, or FDA, and the European Medicines Agency, or EMA. Prior to IGNITE4, we conducted IGNITE1, a phase 3 clinical trial of twice daily IV eravacycline (1.0 mg/kg every 12 hours) compared with ertapenem (1.0g IV every 24 hours) for the treatment of cIAI. In IGNITE1, eravacycline met the primary endpoint of statistical non-inferiority of clinical response.

On January 2, 2018, we announced the submission of a new drug application, or NDA, to the FDA for IV eravacycline for the treatment of cIAI. The NDA submission includes data from the IGNITE1 and IGNITE4 phase 3 clinical trials. In the third quarter of 2017 we submitted a marketing authorization application, or MAA, to the EMA for IV eravacycline for the treatment of cIAI primarily based upon the results of IGNITE1. In February 2018, the FDA notified us that it had completed its initial 60-day review of our NDA and August 28, 2018 was set as the Prescription Drug User Fee Act, or PDUFA, goal date for the FDA's completion of its review of our NDA.

The FDA has granted Qualified Infectious Disease Product (QIDP) and Fast Track designations for IV eravacycline for cIAI.

In February 2018, we announced top-line data from our IGNITE3 trial, a global phase 3 randomized, multi-center, double-blind, clinical trial evaluating the efficacy and safety of once-daily intravenous, or IV, eravacycline, at a dose of 1.5mg/kg every 24 hours, compared to ertapenem, at a dose of 1g every 24 hours, for the treatment of complicated urinary tract infections, or cUTI, that we conducted in 1,205 patients who were randomized 1:1 to receive eravacycline or ertapenem for a minimum of 5 days, and then were eligible for transition to an appropriate approved oral agent. In this trial, eravacycline did not meet the co-primary endpoints of responder rate, a combination of clinical cure and microbiological success, the microbiological intent-to-treat, or micro-ITT, population at the end-of-IV treatment visit and at the test-of-cure visit (5-10 days post therapy). These endpoints were evaluated using a 10% non-inferiority margin. Given the IGNITE3 results, we are no longer evaluating IV eravacycline for the treatment of cUTI and have also ceased development of an oral formulation for eravacycline for the treatment of cUTI.

Eravacycline is designed to treat a broad range of infections, including infections due to multidrug-resistant bacteria. In *in vitro* experiments, eravacycline has demonstrated the ability to cover a wide variety of multidrug-resistant Gram-negative, Gram-positive, anaerobic and atypical bacteria, including multidrug-resistant *Klebsiella pneumoniae* and multi-drug resistant *Acinetobacter.* Multidrug-resistant *Klebsiella pneumoniae* is one of the carbapenem-resistant *Enterobacteriaceae* (or CREs) listed as an urgent threat and multi-drug resistant *Acinetobacter* is listed as a serious threat by the Centers for Disease Control and Prevention, or CDC, in a September 2013 report and they are listed as Priority 1; Critical pathogens in the World Health Organization's priority pathogens list for R&D, published in February 2017. CREs were a confirmed area of great concern by the World Health Organization in an April 2014 global surveillance report. Gram-negative bacteria that are resistant to multiple available antibiotics are increasingly common and a growing threat to public health. We believe that the ability of eravacycline to cover multidrug-resistant Gram-negative bacteria, as well as multidrug-resistant Gram-positive, anaerobic and atypical bacteria, will enable eravacycline to become the drug of choice for first-line empiric treatment of patients with cIAI.

In addition, we are developing TP-6076, a fully-synthetic fluorocycline derivative, as a lead candidate under our second-generation program to target unmet medical needs, including multidrug-resistant Gram-negative bacteria. In June 2017, we announced positive results from a phase 1 randomized, placebo-controlled, double-blind, single-ascending dose study evaluating the safety, tolerability and pharmacokinetics of IV TP-6076. In the study, TP-6076 was well tolerated, and there were no serious or severe adverse events, or discontinuations due to an adverse event. There were no clinically significant safety findings in any laboratory assessments, vital signs, ECGs or physical examinations. We also are conducting a multiple-ascending study in healthy volunteers of the IV formulation of TP-6076.

We commenced business operations in July 2006. Our operations to date have been limited to organizing and staffing our company, business planning, raising capital, acquiring and developing our proprietary chemistry technology, identifying potential product candidates and undertaking preclinical studies and clinical trials of our product candidates. To date, we have not generated any product revenue and have primarily financed our operations through public offerings and private placements of our equity securities, debt financings and funding from the United States government. As of December 31, 2017, we had received an aggregate of $553 million in net proceeds from the issuance of equity securities and borrowings under debt facilities and an aggregate of $49.9 million from government grants and contracts. As of December 31, 2017, our principal source of liquidity was cash and cash equivalents, which totaled $136.4 million.

As of December 31, 2017, we had an accumulated deficit of $461.9 million. Our net losses were $114.8 million, $77.5 million and $83.2 million for the years ended December 31, 2017, 2016 and 2015, respectively. We expect that our expenses will decrease in 2018 compared with 2017, as the completion of the IGNITE clinical program will offset cost increases associated with conducting pre-commercialization activities for eravacycline and, if approved, the launch of eravacycline. If we obtain marketing approval for eravacycline, we do expect to incur significant sales, marketing, distribution and outsourced manufacturing expenses.

We believe that our available funds will be sufficient to support our operations through the first half of 2019, which we believe will allow us to fund the initial launch of IV eravacycline for the treatment of cIAI. We will be required to obtain further funding through public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources to fund our operations including ongoing spending to commercialize eravacycline. Adequate additional financing may not be available to us on acceptable terms, or at all. Our failure to raise capital as and when needed would have a negative impact on our financial condition and our ability to pursue our business strategy. Moreover, we will need to generate significant revenue to achieve profitability, and we may never do so. It is also possible that we will not achieve the progress that we expect with respect to the eravacycline launch, if approved.

**Financial overview**

***Contract and Grant Revenue***

We have derived all of our revenue to date from funding provided under four U.S. government awards for the development of our compounds as potential counter measures for the treatment of disease caused by bacterial biothreat pathogens through our collaborator CUBRC Inc., or CUBRC, an independent, not-for-profit, research corporation that specializes in U.S. government-based contracts and from Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator, or CARB-X, an international public-private partnership focused on advancing new antimicrobial products to address the threat of antibiotic resistance:

- We have received funding for our lead product candidate, eravacycline, under an award from the Biomedical Advanced Research and Development Authority, or BARDA, an agency of the U.S. Department of Health and Human Services. In January 2012, BARDA awarded CUBRC an initial five-year contract, which has been extended, that provides for up to a total of $67.3 million in funding for the development, manufacturing and clinical evaluation of eravacycline for the treatment of disease caused by bacterial biothreat pathogens. We refer to this contract as the BARDA Contract. The funding under the BARDA Contract is also being used for the development, manufacturing and clinical evaluation of eravacycline to treat certain infections caused by life-threatening multidrug-resistant bacteria. We refer to this contract as the BARDA Contract.
- We have received funding for TP-271 under two awards from the National Institute of Allergy and Infectious Diseases, or NIAID, a division of National Institutes of Health, for the development, manufacturing and clinical evaluation of TP-271 for respiratory diseases caused by biothreat and antibiotic-resistant public health pathogens, as well as bacterial pathogens associated with community-acquired bacterial pneumonia:
    - a grant awarded to CUBRC in July 2011 that provides up to a total of approximately $2.9 million through May 31, 2017, when it expired, which we refer to as the NIAID Grant; and
    - a contract awarded to CUBRC in September 2011 that provides up to a total of approximately $35.8 million in funding through March 31, 2019, which we refer to as the NIAID Contract.

We are collaborating with CUBRC on these grants and subcontracts, because when we initially decided to seek government funding, we recognized that we did not have any expertise in bidding for, administrating or managing government-funded contracts. CUBRC serves as the prime contractor under the BARDA Contract, the NIAID Grant and the NIAID Contract, primarily carrying out a program management and administrative role with additional responsibility for the management of preclinical studies. We serve as lead technical expert on all aspects of these awards and also serve as a subcontractor responsible for management of chemistry, manufacturing and control activities and clinical studies. We derive all of our revenue under these collaborations through subcontracts with, and a subaward from, CUBRC, with the flow of funds following the respective activities being conducted by us and by CUBRC.

- In connection with the BARDA Contract, in February 2012, we entered into a cost-plus-fixed-fee subcontract with CUBRC which currently expires on September 30, 2018 under which we may receive funding of up to approximately $41.9 million, reflecting the portion of the BARDA Contract funding that may be paid to us for our activities.
- In connection with the NIAID Contract, in October 2011, we entered into a cost-plus-fixed-fee subcontract with CUBRC which currently expires on March 31, 2019 under which we may receive funding of up to approximately $16.9 million, reflecting the portion of the NIAID Contract funding that may be paid to us for our activities.
- In connection with the NIAID Grant, in November 2011, CUBRC awarded us an initial 55-month, no-fee subaward which was extended and expired on May 31, 2017 under which we received funding of up to approximately $0.9 million, reflecting the portion of the NIAID Grant funding that was paid to us for our activities.

Although the BARDA Contract and our subcontract with CUBRC under the BARDA Contract have terms which currently expire on September 30, 2018, BARDA is entitled to terminate the project for convenience at any time, and is not obligated to provide continued funding beyond current-year amounts from congressionally approved annual appropriations. To the extent that BARDA ceases to provide funding of the program to CUBRC, CUBRC has the right to cease providing funding to us. Committed funding from CUBRC under our BARDA subcontract is up to $41.9 million from the initial contract date through September 30, 2018, of which $35.7 million had been received through December 31, 2017.

Similarly, although the NIAID Contract and our subcontract with CUBRC under the NIAID Contract have terms which currently expire on March 31, 2019, NIAID is entitled to terminate the project for convenience at any time, and is not obligated to provide continued funding beyond March 31, 2019. To the extent NIAID ceases to provide funding of the programs to CUBRC, CUBRC has the right to cease providing funding to us. Committed funding from CUBRC under our subcontract with respect to the NIAID Contract is for up to $16.9 million, from the initial contract date through March 31, 2019, of which $13.2 million had been received through December 31, 2017.

In March 2017, the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator, or CARB-X, an international public-private partnership focused on advancing new antimicrobial products to address the threat of antibiotic resistance, selected us to receive up to $4.0 million in research funding over 18 months for TP-6076. In connection with this funding, we entered into a cost reimbursement Sub-Award Agreement with the Trustees of Boston University, the administrator of the program. We began recognizing revenue from the Sub-Award Agreement in April 2017. Of the $4.0 million in committed funding, $44,000 has been received through December 31, 2017. Although the Sub-Award Agreement has a term which currently expires on December 31, 2018, the project can be terminated for convenience at any time.

We have no products approved for sale. Other than the government funding described above, we do not expect to receive any revenue from any product candidates that we develop, including eravacycline, until we obtain regulatory approval and commercialize such products or until we potentially enter into collaborative agreements with third parties for the development and commercialization of such product candidates. We continue to pursue government funding for other preclinical and clinical programs. If our development efforts for any of our product candidates result in clinical success and regulatory approval, or collaboration agreements with third parties, we may generate revenue from those product candidates.

We expect that our revenue will be less than our expenses for the foreseeable future and that we will experience continued losses as we continue our development of, and seek regulatory approvals for, our product candidates, and begin to commercialize any approved products. Even if we are able to generate revenue from the sale of one or more products, we may not become profitable.

***Research and Development Expenses***

Research and development expenses consist primarily of costs incurred for the research and development of our preclinical and clinical candidates, and include:

- personnel-related expenses, including salaries, benefits and stock-based compensation expense;

- expenses incurred under agreements with contract research organizations, contract manufacturing organizations, and consultants that provide preclinical, clinical, regulatory and manufacturing services;
- payments made under our license agreement with Harvard University;
- the cost of acquiring, developing and manufacturing clinical trial materials and lab supplies;
- facility, depreciation and other expenses, which include direct and allocated expenses for rent, maintenance of our facilities, insurance and other supplies; and
- costs associated with preclinical, regulatory and medical affair activities.

We expense research and development costs to operations as incurred. We recognize costs for certain development activities, such as clinical trials, based on an evaluation of the progress to completion of specific tasks using data such as patient enrollment, clinical site activations or information provided to us by our vendors.

We track external development expenses and personnel expense on a program-by-program basis and allocate common expenses, such as scientific consultants and laboratory supplies, to each program based on the personnel resources allocated to such program. Expenses related to facilities, consulting, travel, conferences, stock-based compensation and depreciation are not allocated to a program and are separately classified as other research and development expenses. The following table identifies research and development expenses on a program-specific basis for our product candidates for the years ended December 31, 2017, 2016 and 2015:

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2017 | 2016 | 2015 |
| | (in thousands) | | |
| Eravacycline | $ 75,541 | $ 37,430 | $ 48,368 |
| BARDA Contract | 5,235 | 2,394 | 10,280 |
| NIAID Contract and NIAID Grant | 3,131 | 1,870 | 890 |
| TP-6076 | 3,348 | 5,517 | 3,232 |
| CARB-X | 715 | - | - |
| Other development programs | 1,186 | 2,196 | 619 |
| Other research and development | 12,550 | 14,357 | 10,379 |
| Total research and development | $ 101,706 | $ 63,764 | $ 73,768 |

Research and development activities are central to our business model. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials.

As of December 31, 2017, we had incurred an aggregate of $256.3 million in research and development expenses related to the development of eravacycline, and $36.3 million in research and development expenses related to the development of eravacycline that were funded under the BARDA Contract. We expect that our research and development expenses will decrease as we complete the IGNITE program for eravacycline.

Because of the numerous risks and uncertainties associated with product development, however, we cannot determine with certainty the duration and completion costs of current or future clinical trials of eravacycline or our other product candidates. We may never succeed in achieving regulatory approval for eravacycline or any of our other product candidates. The duration, costs and timing of clinical trials and development of our product candidates will depend on a variety of factors, including the uncertainties of future clinical and preclinical studies, uncertainties in clinical trial enrollment rate and significant and changing government regulation. In addition, the probability of success for each product candidate will depend on numerous factors, including competition, manufacturing capability and commercial viability.

We have licensed our proprietary chemistry technology from Harvard University on an exclusive worldwide basis under a license agreement that we entered into in August 2006. Under our license agreement, we have paid Harvard an aggregate of $6.1 million in upfront license fees and development milestone payments. We have also issued 31,379 shares of our common stock to Harvard under the license agreement. In addition, we have agreed to make payments to Harvard upon the achievement of specified future development and regulatory milestones totaling up to $15.1 million for each licensed product candidate ($4.8 million of which has already been paid with respect to eravacycline), and to pay tiered royalties in the single digits based on annual worldwide net sales, if any, of licensed products, our affiliates and our sublicensees. We are also obligated to pay Harvard a specified share of non-royalty sublicensing revenues that we receive from sublicensees for the grant of sublicenses under the license and to reimburse Harvard for specified patent prosecution and maintenance costs. The next milestone payments due under the license agreement with respect to eravacycline are a $3.0 million payment upon acceptance of our NDA filing by the FDA, which occurred in February 2018, and a payment due under our Everest license agreement.

***General and Administrative Expenses***

General and administrative expenses consist principally of personnel-related costs, including salaries and related costs such as benefits and stock-based compensation for personnel in executive, finance, operational, corporate communications, marketing and human resource functions. Other significant general and administrative expenses include professional fees for legal, patent, auditing and tax services, consulting, and facility costs not otherwise included in research and development expenses.

We anticipate that our general and administrative expenses will increase for a number of reasons, including:

- support of the anticipated expansion of our research and development activities as we continue the development of our product candidates;
- expansion of infrastructure, including increases in personnel-related costs, consulting, legal, and accounting costs, and directors and officers insurance premiums; and
- if and when we believe a regulatory approval of our first product candidate appears likely, anticipated increases in our personnel-related and consulting costs as a result of our preparation for commercial operations, especially as it relates to the sales and marketing of our product candidates.

***Other Income***

Other income consists primarily of interest income earned on our cash and cash equivalents.

**Critical Accounting Policies and Significant Judgments and Estimates**

Our management's discussion and analysis of our financial condition and results of operations are based on our consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, revenues and expenses and the disclosure of contingent assets and liabilities in our financial statements. On an ongoing basis, we evaluate our estimates and judgments, including those related to revenue recognition, accrued clinical expenses, and stock-based compensation. We base our estimates on historical experience, known trends and events and various other factors that we and our management believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in the notes to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K, we believe the following accounting policies to be most critical to the judgments and estimates used in the preparation of our financial statements.

***Revenue Recognition***

We have derived all of our revenue to date from our subcontracts with CUBRC under the BARDA Contract and the NIAID Contract, our subaward under the NIAID Grant and our award from CARB-X. We recognize revenue under these best-efforts, cost-reimbursable and cost-plus-fixed-fee arrangements as we perform services under the arrangements so long as an arrangement has been executed and the fees for these services are fixed or determinable, legally billable and reasonably assured of collection. Recognized amounts reflect our partial performance under the subcontracts and subaward and equal direct and indirect costs incurred plus fixed fees, where applicable. We do not recognize revenue under these arrangements for amounts related to contract periods where funding is not yet committed as amounts above committed funding thresholds would not be considered fixed or determinable or reasonably assured of collection. Revenues and expenses under these arrangements are presented gross on our statements of operations and comprehensive loss as we have determined we are the primary obligor under these arrangements relative to the research and development services we perform as lead technical expert.

Revenue under our subcontracts under both the NIAID Contract and the BARDA Contract are earned under a cost-plus-fixed-fee arrangement in which we are reimbursed for direct costs incurred plus allowable indirect costs and a fixed-fee earned. Billings under these contracts are based on approved provisional indirect billing rates, which permit recovery of fringe benefits, allowable overhead and general and administrative expenses and a fixed fee.

Revenue under our subaward under the NIAID Grant and the CARB-X Award are earned under a cost-reimbursable arrangement in which we are reimbursed for direct costs incurred plus allowable indirect costs. Billings under the NIAID Grant and CARB-X Award are based on approved provisional indirect billing rates, which permit recovery of fringe benefits and allowable general and administrative expenses.

***Accrued Research and Development Expenses***

As part of the process of preparing our financial statements, we are required to estimate our accrued expenses. This process involves reviewing open contracts and purchase orders, communicating with our personnel to identify services that have been performed for us and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. The majority of our service providers invoice us monthly in arrears for services performed or when contractual milestones are met. We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. Examples of estimated accrued research and development expenses include fees paid to:

- contract research organizations in connection with the conduct of our clinical trials;
- contract manufacturing organizations with respect to the manufacture of drug supply for clinical trials and manufacture of drug substance and finished product; and
- vendors and consultants in connection with preclinical development activities.

We base our expenses related to clinical studies on our estimates of the services completed and efforts expended pursuant to contracts with multiple contract research organizations that conduct and manage clinical studies on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the clinical expense. Payments under some of these contracts depend on factors such as the successful enrollment of subjects and the completion of clinical trial milestones. In accruing service fees, we estimate the time period over which services will be performed, enrollment of subjects, number of sites activated and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or prepaid accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, if our estimates of the status and timing of services performed differ from the actual status and timing of services performed we may report amounts that are too high or too low in any particular period. To date, there have been no material differences from our estimates to the amount actually incurred.

***Stock-Based Compensation***

We apply the fair value recognition provisions of Financial Accounting Standards Board Accounting Standards Codification Topic 718, *Compensation-Stock Compensation*, or ASC 718, to account for all stock-based compensation. We recognize compensation costs related to stock options and restricted stock units granted to employees based on the estimated fair value of the awards on the date of grant. Stock compensation related to non-employee awards is remeasured at each reporting period until the awards are vested.

Determining the amount of stock-based compensation to be recorded requires us to develop estimates of the fair value of stock-based awards as of their grant date for awards granted to employees and as of their measurement date for awards granted to non-employees. For awards granted to employees, we recognize stock-based compensation expense ratably over the requisite service period, which in most cases is the vesting period of the award. For awards granted to non-employees, we recognize stock-based compensation expense over the requisite service period using the accelerated attribution method. Calculating the fair value of stock-based awards requires that we make subjective assumptions.

We use the Black-Scholes option pricing model to value our stock option awards. Use of this valuation methodology requires that we make assumptions as to the volatility of our common stock, the expected term of our stock options, the risk free interest rate for a period that approximates the expected term of our stock options and our expected dividend yield. Since we completed our IPO on March 25, 2013, we have not had sufficient historical data to support a calculation of volatility and expected life. As such, we have used a weighted-average volatility considering our own volatility and the volatilities of a representative group of publicly traded companies. For purposes of identifying similar entities, we selected a group of publicly traded life science/biotechnology companies based on their disease focus, stage of development, number of compounds in clinical trials and number of years as a publicly-traded company. We use the simplified method as prescribed by the Securities and Exchange Commission Staff Accounting Bulletin No. 107, *Share-Based Payment* as we do not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term of stock options granted to employees. For non-employee grants, we use an expected term equal to the remaining contractual term of the award. We utilize a dividend yield of zero based on the fact that we have never paid cash dividends and have no current intention of paying cash dividends. The risk-free interest rate used for each grant is based on the U.S. Treasury yield curve in effect at the time of measurement for instruments with a similar expected term.

In May 2017, the Financial Accounting Standards Board, or FASB issued Accounting Standards Update, or ASU, No. 2017-09, which provides guidance about which changes to the terms or conditions of a share-based payment award require an entity to apply modification accounting in Topic 718. The new standard will be effective on January 1, 2018. We are currently evaluating the potential impact that this standard may have on our financial position, statements of operations and cash flows.

**Results of Operations**

***Comparison of Years Ended December 31, 2017 and 2016***

The following tables summarize the results of our operations for each of the years ended December 31, 2017 and 2016, together with the changes in those items in dollars and as a percentage:

| | Years Ended December 31, | | Increase/ | |
|---|---|---|---|---|
| | 2017 | 2016 | (decrease) | % |
| | (in thousands) | | | |
| Revenues | $ 9,666 | $ 5,145 | $ 4,521 | 88% |
| Operating expenses: | | | | |
| Research and development | 101,706 | 63,764 | 37,942 | 60% |
| General and administrative | 23,675 | 19,211 | 4,464 | 23% |
| Total operating expenses | 125,381 | 82,975 | 42,406 | 51% |
| Loss from operations | (115,715) | (77,830) | (37,885) | 49% |
| Other income (expense) | 963 | 350 | 613 | 175% |
| Net loss | $ (114,752) | $ (77,480) | $ (37,272) | 48% |

*Revenue from U.S. Government Contracts and Grants*

The following table sets forth our contract and grant revenue for the years ended December 31, 2017 and 2016:

| Revenue | Years Ended December 31, 2017 | 2016 | Increase/ (decrease) | % |
|---|---|---|---|---|
| | (in thousands) | | | |
| BARDA Contract | $ 5,463 | $ 2,879 | $ 2,584 | 90% |
| NIAID Contract | 3,509 | 2,164 | 1,345 | 62% |
| CARB-X Award | 685 | — | 685 | — |
| NIAID Grant | 9 | 102 | (93) | (91)% |
| | $ 9,666 | $ 5,145 | $ 4,521 | 88% |

Contract and grant revenue was $9.7 million for the year ended December 31, 2017 compared to $5.1 million for the year ended December 31, 2016, an increase of $4.5 million, or 88%. This increase was primarily due to changes in the timing and scope of activities under our subcontracts with respect to the BARDA and NIAID Contracts conducted during the year ended December 31, 2017 as compared to the year ended December 31, 2016 and the addition of amounts received under the CARB-X Award.

*Research and Development Expenses*

Research and development expenses were $101.7 million for the year ended December 31, 2017 compared to $63.8 million for the year ended December 31, 2016, an increase of $37.9 million, or 60%. The increase was primarily due to costs associated with conducting our IGNITE3 and IGNITE4 phase 3 clinical trials and an increase in regulatory costs associated with eravacycline related to our MAA and NDA filing activities.

*General and Administrative Expenses*

General and administrative expenses for the year ended December 31, 2017 were $23.7 million compared to $19.2 million for the year ended December 31, 2016, an increase of $4.5 million, or 23%. This increase was primarily due to an increase in pre-launch commercial and business development expenses and headcount related costs.

*Other Income*

Other income consisted of interest income for the year ended December 31, 2017 was $1.0 million compared to $0.3 for the year ended December 31, 2016, driven by the larger cash balance from our follow-on public offering and sales under our "at-the-market" offering program in 2017.

***Comparison of Years Ended December 31, 2016 and 2015***

The following tables summarize the results of our operations for each of the years ended December 31, 2016 and 2015, together with the changes in those items in dollars and as a percentage:

| | Years Ended December 31, 2016 | 2015 | Increase/ (decrease) | % |
|---|---|---|---|---|
| | (in thousands) | | | |
| Revenues | $ 5,145 | $ 11,686 | $ (6,541) | (56)% |
| Operating expenses: | | | | |
| Research and development | 63,764 | 73,768 | (10,004) | (14)% |
| General and administrative | 19,211 | 20,916 | (1,705) | (8)% |
| Total operating expenses | 82,975 | 94,684 | (11,709) | (12)% |
| Loss from operations | (77,830) | (82,998) | 5,168 | (6)% |
| Other income (expense) | 350 | (191) | 541 | (283)% |
| Net loss | $ (77,480) | $ (83,189) | $ 5,709 | (7)% |

*Revenue from U.S. Government Contracts and Grants*

The following table sets forth our contract and grant revenue for the years ended December 31, 2016 and 2015:

| Revenue | Years Ended December 31, 2016 | 2015 | Increase/ (decrease) | % |
|---|---|---|---|---|
| | | (in thousands) | | |
| BARDA Contract | $ 2,879 | $ 10,773 | $ (7,894) | (73)% |
| NIAID Contract | 2,164 | 756 | 1,408 | 186% |
| NIAID Grant | 102 | 157 | (55) | (35)% |
| | $ 5,145 | $ 11,686 | $ (6,541) | (56)% |

Contract and grant revenue was $5.1 million for the year ended December 31, 2016 compared to $11.7 million for the year ended December 31, 2015, a decrease of $6.6 million, or 56%. This decrease was primarily due to changes in the timing and scope of activities conducted under our subcontract with respect to the BARDA Contract during the year ended December 31, 2016 as compared to the year ended December 31, 2015, offset in part by the timing and scope of activities conducted under our subcontract with respect to the NIAID Contract.

*Research and Development Expenses*

Research and development expenses were $63.8 million for the year ended December 31, 2016 compared to $73.8 million for the year ended December 31, 2015, a decrease of approximately $10.0 million, or 14%. This decrease was primarily due to a decrease in clinical trial costs associated with the completion of IGNITE2, a decrease in certain pre-clinical registration activities for eravacycline and a decrease in drug manufacturing costs under our BARDA sub-contract. These decreases were offset in part by costs associated with the initiation of IGNITE2 and IGNITE4, an increase in personnel-related costs due to additional headcount and an increase in stock-based compensation expense resulting from additional headcount and our annual stock option awards and restricted stock units granted to employees during the first quarter of 2016.

*General and Administrative Expenses*

General and administrative expenses for the year ended December 31, 2016 were $19.2 million compared to $20.9 million for the year ended December 31, 2015, a decrease of $1.7 million, or 8%. This decrease was primarily due to a decrease in market research and pre-commercialization expenses. This decrease was offset by an increase in stock-based compensation primarily due a non-employee stock-based compensation credit during 2015 and an increase in legal fees.

*Other Income (Expense)*

Other income for the year ended December 31, 2016 consisted of interest income of $0.3 million as compared to $42,000 for the year ended December 31, 2015. The increase was driven by implementation of a new cash sweep account and improved overall yields on our money market funds. Other expense for the year ended December 31, 2015 consisted of interest expense of $0.2 million related to our term loan facility with Silicon Valley Bank and Oxford Finance. These facilities were paid in full on March 31, 2015 and therefore there was no interest expense for the year ended December 31, 2016.

**Liquidity and Capital Resources**

We have incurred losses since our inception and anticipate that we will continue to incur losses for at least the next several years. We expect that our total expenses to decrease but remain significant in 2018 and, as a result, we will need additional capital to fund our operations, which we may obtain from additional financings, research funding, collaborations, contract and grant revenue or other sources.

Since our inception, we have funded our operations principally through the receipt of funds from public offerings and private placements of equity securities, debt financings and contract research funding and research grants from the United States government.

As of December 31, 2017, we had cash and cash equivalents of approximately $136.4 million. We invest cash in excess of immediate requirements in accordance with our investment policy, primarily with a view to liquidity and capital preservation. As of December 31, 2017, our funds were held in cash and money market funds.

On March 17, 2015, we completed the sale of 4,945,000 shares of common stock in a follow-on public offering at a price to the public of $35.00 per share, which number of shares includes the underwriters' exercise in full of their option to purchase additional shares. This offering resulted in net proceeds to us of $162.2 million after deducting underwriting discounts and commissions of $10.4 million and offering costs of $0.5 million.

On January 17, 2017, we entered into a Controlled Equity Offering Sales Agreement, or sales agreement, with Cantor Fitzgerald & Co., as sales agent, or Cantor. On July 7, 2017, we entered into an amendment to the sales agreement, or the amended sales agreement. In accordance with the terms of the sales agreement, we may offer and sell through Cantor, from time to time, shares of our common stock up to an aggregate offering price of $80,000,000 through an "at-the-market" offering program. As of December 31, 2017, we had sold 4,157,873 shares under the Agreement at an average price of $7.78 per share and we had received aggregate cash proceeds of $31.1 million, after deducting the sales commissions and offering expenses. Under the Sales Agreement, Cantor may sell shares of our common stock by methods deemed to be an "at-the-market" offering as defined in Rule 415 promulgated under the Securities Act of 1933, as amended, including sales made directly on The NASDAQ Global Select Market or on any other existing trading market for our common stock. We are not obligated to make any sales of shares of our common stock under the Sales Agreement. We or Cantor may suspend or terminate the offering of shares of our common stock upon notice to the other party and subject to other conditions. We will pay Cantor a commission rate equal to 3.0% of the gross proceeds per share sold.

On August 2, 2017, we sold 10,000,000 shares of common stock in an underwritten public offering at an offering price to the public of $6.50 per share, resulting in net proceeds to us of $60.7 million after deducting underwriting discounts and commissions of $3.9 million and offering costs of $0.4 million. In connection with the offering, we granted the underwriters an option to purchase up to an additional 1,500,000 shares on the same terms and conditions as the offering, pursuant to which the underwriters exercised an option to purchase 107,000 additional shares on August 25, 2017 resulting in additional net proceeds to us of approximately $0.7 million after deducting underwriting discounts and commissions.

The following table summarizes our sources and uses of cash for each of the periods set forth below:

| | Years Ended December 31, | | |
|---|---|---|---|
| | 2017 | 2016 | 2015 |
| | (in thousands) | | |
| Net cash used in operating activities | $ (98,050) | $ (63,766) | $ (76,707) |
| Net cash used in investing activities | (771) | (393) | (838) |
| Net cash provided by financing activities | 93,146 | 333 | 162,415 |
| Net increase (decrease) in cash and cash equivalents | $ (5,675) | $ (63,826) | $ 84,870 |

During the years ended December 31, 2017, 2016 and 2015, our operating activities used net cash of $98.1 million, $63.8 million and $76.7 million, respectively. Net cash used by operating activities for the year ended December 31, 2017 increased by $34.3 million compared to the year ended December 31, 2016. The increase is primarily due to an increase in expenses related to our eravacycline Phase 3 clinical studies and higher drug manufacturing and nonclinical costs in support of our NDA-related and pre-commercialization activities for eravacycline. Net cash used in operating activities for the year ended December 31, 2016 decreased by $12.9 million compared to the year ended December 31, 2015. The decrease is primarily due to a net decrease in expenses related to our eravacycline Phase 3 clinical studies and lower drug manufacturing and nonclinical costs in support of our NDA-related and pre-commercialization activities for eravacycline.

During the years ended December 31, 2017, 2016 and 2015, our investing activities used net cash of $0.8 million, $0.4 million and $0.8 million, respectively. The net cash used in investing activities during these periods resulted from purchases of property, plant and equipment to facilitate our increased research and development activities and increased headcount.

During the years ended December 31, 2017, 2016 and 2015 our net cash provided by financing activities was $93.1 million, $0.3 million and $162.4 million, respectively. The net cash provided by financing activities during the year ended December 31, 2017 was primarily due to sales of common stock under our amended sales agreement with Cantor Fitzgerald and our August 2017 follow-on public offering. The net cash provided by financing activities during the year ended December 31, 2016 primarily reflected proceeds from the issuance of stock under our stock plans. The net cash provided by financing activities during the year ended December 31, 2015 primarily reflected proceeds from our March 2015 follow-on public offering of $162.2 million, as well as proceeds from the exercise of stock options of $4.9 million, offset in part by repayment of the remaining indebtedness under our term loan facility with Silicon Valley Bank and Oxford Finance of $4.6 million.

***Operating Capital Requirements***

We expect to incur significant operating losses for at least the next several years as we continue development of eravacycline, seek marketing approval for eravacycline, manufacture drug product for our clinical and pre-clinical trials, conduct pre-commercialization and launch-related activities for eravacycline, conduct our phase 1 clinical trial of TP-271in healthy volunteers, and our phase 1 clinical trial of TP-6076 in healthy volunteers and satisfy our obligations under our license agreement with Harvard University. We may not be able to complete the development and initiate commercialization of eravacycline or our other product candidates if, among other things, our preclinical research and clinical trials with respect to our other product candidates are not successful, our manufacturing efforts are not successful, the FDA or the EMA does not approve eravacycline or our other product candidates when we expect, or at all.

We believe that our available funds will be sufficient to support our operations through the first half of 2019, which we believe will allow us to fund the initial launch of IV eravacycline for the treatment of cIAI. We will be required to obtain further funding through public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources to fund our operations including ongoing spending to commercialize eravacycline.

We have based our projections of operating capital requirements on assumptions that may prove to be incorrect and we may use all of our available capital resources sooner than we expect. Because of the numerous risks and uncertainties associated with research, development and commercialization of pharmaceutical products, we are unable to estimate the exact amount of our operating capital requirements. Our future funding requirements will depend on many factors, including, but not limited to:

- the outcome, timing and costs of seeking regulatory approvals;
- costs related to the anticipated commercial launch of eravacycline;
- revenue received from commercial sales of eravacycline, subject to receipt of marketing approval;
- the initiation, progress, timing, costs and results of preclinical studies and clinical trials for our other product candidates and potential product candidates;
- the amount of funding that we receive under our subcontracts under the BARDA and NIAID Contracts, and the activities funded under the BARDA Contract, the NIAID Contract and our agreement with CARB-X;
- the number and characteristics of product candidates that we pursue;
- the costs of commercialization activities for other product candidates if we receive marketing approval, including the timing and costs of establishing product sales, marketing, distribution and manufacturing capabilities;
- the terms and timing of any future collaborations, licensing, consulting or other arrangements that we may establish, as we did with Everest Medicines;
- the amount and timing of any payments we may be required to make, or that we may receive, in connection with the licensing, filing, prosecution, defense and enforcement of any patents or other intellectual property rights, including milestone and royalty payments and patent prosecution fees that we are obligated to pay to Harvard pursuant to our license agreement;
- the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against intellectual property related claims; and
- the extent to which we in-license or acquire other products and technologies.

We expect that we will need to obtain substantial additional funding in order to commercialize eravacycline. To the extent that we raise additional capital through the sale of common stock, convertible securities or other equity securities, the ownership interests of our existing stockholders may be materially diluted and the terms of these securities could include liquidation or other preferences that could adversely affect the rights of our existing stockholders. In addition, debt financing, if available, would result in increased fixed payment obligations and may involve agreements that include restrictive covenants that limit our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends, that could adversely impact our ability to conduct our business. If we are unable to raise capital when needed or on attractive terms, we could be forced to significantly delay, scale back or discontinue the development or commercialization of eravacycline or other product candidates, seek collaborators at an earlier stage than otherwise would be desirable or on terms that are less favorable than might otherwise be available, and relinquish or license, potentially on unfavorable terms, our rights to eravacycline or other product candidates that we otherwise would seek to develop or commercialize ourselves.

**Contractual Obligations and Commitments**

The following table summarizes our outstanding contractual obligations as of payment due date by period at December 31, 2017:

| | Payment due by period | | | | |
|---|---|---|---|---|---|
| **Contractual Obligations** | **Total** | **Less than 1 Year** | **1 -3 Years** | **3-5 Years** | **More than 5 Years** |
| | | | **(in thousands)** | | |
| Operating leases (1) | $ 3,402 | $ 1,752 | $ 1,650 | $ - | $ - |
| Harvard milestone payment (2) | 7,750 | 7,750 | - | - | - |
| Total contractual cash obligations | $ 11,152 | $ 9,502 | $ 1,650 | $ - | $ - |

(1) On June 18, 2015, we amended our existing operating lease to expand our leased premises under that lease to a total of 37,438 square feet, and we also extended our lease term through November 30, 2019. In third quarter of 2016, we entered into a sublease with respect to a portion of our principal facilities, which consist of office, research and laboratory space located at 480 Arsenal Way, Watertown, Massachusetts, with an unrelated third party. The term of the sublease expires in November 2019, with the sublessee obligated to pay rent to us that approximates the rent we are currently paying to our landlord with respect to such portion of the facility.

(2) Consists of milestone payments that would become due to Harvard of (i) $3.0 million upon acceptance by the FDA of an NDA filing for eravacycline, which occurred in February 2018, (ii) $1.8 million upon approval by the EMA of MAA filing for eravacycline, and (iii) $3.0 million upon approval by the FDA of our NDA filing for eravacycline. We cannot determine the exact timing of payment of these milestones, or if they would ever become due at all.

We are contractually obligated under our license agreement with Harvard University to make payments to Harvard upon the achievement of specified future development and regulatory milestones totaling up to $15.1 million for each licensed product candidate $4.8 million of which has already been paid with respect to eravacycline), and to pay tiered royalties in the single digits based on annual worldwide net sales, if any, of licensed products by us, our affiliates and sublicensees. We are also obligated to pay Harvard a specified share of non-royalty sublicensing revenue that we receive from sublicensees for the grant of sublicenses under the license and to reimburse Harvard for specified patent prosecution and maintenance costs. Many of these potential payments are contingent upon the occurrence of certain future events and, given the nature of those events, it is unclear when, if ever, we may be required to pay such amounts or what the total amount of such payments will be. Except for the milestone payments referenced in the contractual obligations table and described in the footnote above, the table does not include any other potential milestone or royalty payments to Harvard.

We have employment agreements with certain employees which require the funding of a specific level of payments, if certain events, such as a change in control or termination without cause, occur.

In the course of normal business operations, we also have agreements with contract service providers to assist in the performance of our research and development and manufacturing activities. We can elect to discontinue the work under these agreements at any time. We could also enter into additional collaborative research, contract research, manufacturing, and supplier agreements in the future, which may require up-front payments and even long-term commitments of cash.

**Off-Balance Sheet Arrangements**

We did not have, during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined under applicable SEC rules.

**ITEM 7A. Quantitative and Qualitative Disclosures About Market Risk**

We are exposed to market risk related to changes in interest rates. Our cash equivalents consist of money market funds at December 31, 2017 and 2016. The investments in these financial instruments are made in accordance with an investment policy approved by our board of directors which specifies the categories, allocations and ratings of securities we may consider for investment. The primary objective of our investment activities is to preserve principal while at the same time maximizing the income we receive without significantly increasing risk. Some of the financial instruments that we invest in could be subject to market risk. This means that a change in prevailing interest rates may cause the value of the instruments to fluctuate. For example, if we purchase a security that was issued with a fixed interest rate and the prevailing interest rate later rises, the value of that security will probably decline. To minimize this risk, we intend to maintain a portfolio which may include cash, cash equivalents and investment securities available-for-sale in a variety of securities which may include money market funds, government and non-government debt securities and commercial paper, all with various maturity dates. Based on our current investment portfolio, we do not believe that our results of operations or our financial condition would be materially impacted by an immediate change of 10% in interest rates.

We do not hold or issue derivatives, derivative commodity instruments or other financial instruments for speculative trading purposes. Further, we do not believe our cash equivalents and investment securities have significant risk of default or illiquidity. We made this determination based on discussions with our investment advisors and a review of our holdings. While we believe our cash equivalents and investment securities do not contain excessive risk, we cannot provide absolute assurance that in the future our investments will not be subject to adverse changes in market value. All of our investments are recorded at fair value.

**ITEM 8. Financial Statements and Supplementary Data**

**TETRAPHASE PHARMACEUTICALS, INC.**
**INDEX TO CONSOLIDATED FINANCIAL STATEMENTS**

## Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Tetraphase Pharmaceuticals, Inc.

**Opinion on the Financial Statements**

We have audited the accompanying consolidated balance sheets of Tetraphase Pharmaceuticals, Inc. (the Company) as of December 31, 2017 and 2016, the related consolidated statements of operations and comprehensive loss, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2017, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2017 and 2016, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2017, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2017, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) and our report dated March 6, 2018 expressed an unqualified opinion thereon.

**Basis for Opinion**

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2007.
Boston, Massachusetts
March 6, 2018

**Tetraphase Pharmaceuticals, Inc.**
**Consolidated Balance Sheets**

*(In thousands, except par value amounts)*

| | December 31, 2017 | December 31, 2016 |
|---|---|---|
| **Assets** | | |
| Current assets: | | |
| Cash and cash equivalents | $ 136,411 | $ 142,086 |
| Accounts receivable | 4,653 | 1,789 |
| Prepaid expenses and other current assets | 6,382 | 6,582 |
| Total current assets | 147,446 | 150,457 |
| Property and equipment, net | 1,395 | 1,054 |
| Restricted cash | 199 | 199 |
| Total assets | $ 149,040 | $ 151,710 |
| **Liabilities and stockholders' equity** | | |
| Current liabilities: | | |
| Accounts payable | $ 5,306 | $ 2,555 |
| Accrued expenses | 12,559 | 7,685 |
| Deferred revenue | 660 | 1,255 |
| Total current liabilities | 18,525 | 11,495 |
| Other long term liabilities | 105 | 162 |
| Commitments and contingencies (Note 10) | | |
| Stockholders' equity: | | |
| Preferred stock, par value $0.001 per share; 5,000 shares authorized; no shares issued and outstanding | — | — |
| Common stock, par value $0.001 per share; 125,000 shares authorized; 51,458 and 36,942 shares issued and outstanding at December 31, 2017 and 2016, respectively | 51 | 37 |
| Additional paid-in capital | 592,243 | 487,148 |
| Accumulated deficit | (461,884) | (347,132) |
| Total stockholders' equity | 130,410 | 140,053 |
| Total liabilities and stockholders' equity | $ 149,040 | $ 151,710 |

*See accompanying notes to consolidated financial statements.*

**Tetraphase Pharmaceuticals, Inc.**
**Consolidated Statements of Operations and Comprehensive Loss**

*(In thousands, except per share data)*

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2017 | 2016 | 2015 |
| **Revenues** | $ 9,666 | $ 5,145 | $ 11,686 |
| **Operating expenses:** | | | |
| Research and development | 101,706 | 63,764 | 73,768 |
| General and administrative | 23,675 | 19,211 | 20,916 |
| Total operating expenses | 125,381 | 82,975 | 94,684 |
| Loss from operations | (115,715) | (77,830) | (82,998) |
| **Other income (expense):** | | | |
| Other income (expense) | 963 | 350 | (191) |
| Other income (expense), net | 963 | 350 | (191) |
| **Net loss** | $ (114,752) | $ (77,480) | $ (83,189) |
| **Net loss per share-basic and diluted** | $ (2.63) | $ (2.11) | $ (2.36) |
| **Weighted-average number of common shares used in net loss per share-basic and diluted** | 43,582 | 36,704 | 35,261 |
| **Comprehensive loss** | $ (114,752) | $ (77,480) | $ (83,189) |

*See accompanying notes to consolidated financial statements.*

**Tetraphase Pharmaceuticals, Inc.**
**Consolidated Statements of Stockholders' Equity**

*(In thousands)*

| | Common Shares | | Additional Paid-In Capital | Accumulated Deficit | Total Stockholders' Equity (Deficit) |
|---|---|---|---|---|---|
| | Shares | Amount | | | |
| **Balance at December 31, 2014** | 30,806 | 31 | 294,998 | (186,463) | 108,566 |
| Issuance of common stock under stock plans | 818 | 1 | 4,671 | — | 4,672 |
| Issuance of common stock from follow-on public offering (net of underwriters discounts and issuance costs) | 4,945 | 5 | 162,146 | — | 162,151 |
| Shares issued in connection with employee stock purchase plan | 16 | — | 239 | — | 239 |
| Stock-based compensation expense | — | — | 11,616 | — | 11,616 |
| Net loss | — | — | — | (83,189) | (83,189) |
| **Balance at December 31, 2015** | 36,585 | 37 | 473,670 | (269,652) | 204,055 |
| Issuance of common stock under stock plans | 298 | — | 146 | — | 146 |
| Shares issued in connection with employee stock purchase plan | 59 | — | 187 | — | 187 |
| Stock-based compensation expense | — | — | 13,145 | — | 13,145 |
| Net loss | — | — | — | (77,480) | (77,480) |
| **Balance at December 31, 2016** | 36,942 | 37 | $ 487,148 | $ (347,132) | $ 140,053 |
| Issuance of common stock under stock plans | 173 | — | 289 | — | 289 |
| Issuance of common stock from follow-on public offering less underwriters discounts and issuance costs | 10,107 | 10 | 61,384 | — | 61,394 |
| Issuance of common stock under "at-the-market" equity offering sales agreement, less issuance costs | 4,158 | 4 | 31,138 | — | 31,142 |
| Issuance of common stock under employee stock purchase plan | 78 | — | 321 | — | 321 |
| Stock-based compensation expense | — | — | 11,963 | — | 11,963 |
| Net loss | — | — | — | (114,752) | (114,752) |
| **Balance at December 31, 2017** | 51,458 | 51 | $ 592,243 | $ (461,884) | $ 130,410 |

*See accompanying notes to consolidated financial statements.*

**Tetraphase Pharmaceuticals, Inc.**

**Consolidated Statements of Cash Flows**

*(In thousands)*

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2017 | 2016 | 2015 |
| **Operating activities** | | | |
| Net loss | $ (114,752) | $ (77,480) | $ (83,189) |
| Adjustments to reconcile net loss to net cash used in operating activities | | | |
| Depreciation and amortization | 431 | 282 | 193 |
| Amortization of deferred financing costs and debt discount | — | — | 94 |
| Accretion of final interest payment on term loans | — | — | 45 |
| Stock-based compensation expense | 11,963 | 13,145 | 11,616 |
| Loss from disposal of property and equipment | — | — | 2 |
| Changes in operating assets and liabilities: | | | |
| Accounts receivable | (2,864) | 2,362 | (693) |
| Prepaid expenses and other assets | 200 | (2,870) | (1,514) |
| Accounts payable | 2,751 | (302) | (1,249) |
| Accrued expenses and other liabilities | 4,816 | 751 | (2,663) |
| Deferred revenue | (595) | 346 | 651 |
| Net cash used in operating activities | (98,050) | (63,766) | (76,707) |
| **Investing activities** | | | |
| Purchases of property and equipment | (771) | (393) | (838) |
| Net cash used in investing activities | (771) | (393) | (838) |
| **Financing activities** | | | |
| Proceeds from sale of common stock, net of underwriter discounts and issuance costs | 92,536 | — | 162,151 |
| Repayment of term loan payable | — | — | (4,646) |
| Proceeds from issuance of stock under stock plans | 610 | 333 | 4,910 |
| Net cash provided by financing activities | 93,146 | 333 | 162,415 |
| Net increase (decrease) in cash and cash equivalents | (5,675) | (63,826) | 84,870 |
| Cash and cash equivalents at beginning of period | 142,086 | 205,912 | 121,042 |
| Cash and cash equivalents at end of period | $ 136,411 | $ 142,086 | $ 205,912 |
| **Supplemental cash flow information** | | | |
| Cash paid for interest | $ - | $ - | $ 363 |

*See accompanying notes to consolidated financial statements.*

## (1) Organization and Operations

***The Company***

Tetraphase Pharmaceuticals, Inc. (the "Company") is a clinical-stage biopharmaceutical company using its proprietary chemistry technology to create novel antibiotics for serious and life-threatening multidrug-resistant infections. The Company is developing its lead product candidate, eravacycline, a fully synthetic fluorocycline, as an intravenous, or IV, antibiotic for use as a first-line empiric monotherapy for the treatment of multidrug-resistant infections, including multidrug-resistant, or MDR, Gram-negative infections.

The Company has conducted a global phase 3 clinical program for eravacycline called IGNITE (**I**nvestigating **G**ram-**N**egative **I**nfections **T**reated with **E**ravacycline).

In January 2018, the Company announced that it had submitted a new drug application, or NDA, for IV eravacycline for the treatment of complicated intra-abdominal infections, or cIAI, to the U.S. FDA based on the positive results from two of its phase 3 clinical trials (IGNITE1 and IGNITE4). In February 2018, the Company announced that the FDA had notified it that the FDA had completed its initial 60-day review of the NDA and August 28, 2018 was set as the Prescription Drug User Fee Act, or PDUFA, goal date for the FDA's completion of its review of the NDA for eravacycline. In the third quarter of 2017, the Company submitted a marketing authorization application, or MAA, to the EMA for IV eravacycline for the treatment of cIAI primarily based upon the results of IGNITE1.

In addition to eravacycline, the Company is pursuing development of TP-271, a fully synthetic fluorocycline being developed for respiratory disease caused by bacterial biothreat pathogens, and TP-6076, a fully synthetic fluorocycline, targeted at unmet medical needs, including multidrug-resistant Gram-negative bacteria. Both these programs are in phase 1. The Company is no longer developing eravacycline (IV or oral formulations) for the treatment of complicated urinary tract infections as a result of the clinical outcomes of IGNITE2 and IGNITE3.

The Company has incurred annual net operating losses in every year since its inception. As of December 31, 2017, the Company had incurred losses since inception of $461.9 million. The Company has not generated any product revenues and has financed its operations primarily through public offerings and private placements of its equity securities, debt financings and funding from the United States government.

There can be no assurance that the Company will be able to obtain additional debt or equity financing or generate product revenue or revenues from collaborative partners, on terms acceptable to the Company, on a timely basis or at all. The failure of the Company to obtain sufficient funds on acceptable terms when needed could have a material adverse effect on the Company's business, results of operations and financial condition.

## (2) Summary of Significant Accounting Policies

***Segment Information***

Operating segments are defined as components of an enterprise about which separate discrete information is available for evaluation by the chief operating decision maker, or decision-making group, in deciding how to allocate resources and in assessing performance. The Company views its operations and manages its business in one operating segment, which is the business of developing and commercializing its proprietary chemistry technology to create novel antibiotics for serious and life-threatening infections, including multidrug-resistant infections.

***Use of Estimates***

The preparation of financial statements in conformity with generally accepted accounting principles ("GAAP") requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities, revenue and expenses, and related disclosures. On an ongoing basis, the Company's management evaluates its estimates, including estimates related to clinical trial accruals, stock-based compensation expense, contract and grant revenues, and expenses. The Company bases its estimates on historical experience and other market-specific or other relevant assumptions that it believes to be reasonable under the circumstances. Actual results may differ from those estimates or assumptions.

***Concentrations of Credit Risk and Off-Balance Sheet Risk***

Financial instruments that potentially subject the Company to concentrations of credit risk are primarily cash, cash equivalents, restricted cash and accounts receivable from CUBRC Inc. ("CUBRC"), an independent, not-for-profit, research corporation that specializes in U.S. government-based contracts, and the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator, or CARB-X, an international public-private partnership focused on advancing new antimicrobial products to address the threat of antibiotic resistance. The Company maintains its cash and cash equivalent balances in the form of cash and money market accounts with financial institutions that management believes are creditworthy. The Company's investment policy includes guidelines on the quality of the institutions and financial instruments and defines allowable investments that the Company believes minimize its exposure to concentration of credit risk. The Company has no financial instruments with off-balance-sheet risk of loss. The company has a strong track record of collection on its accounts receivable from CUBRC. The company's agreement with CARB-X has been in place since 2017.

***Principles of Consolidation***

The condensed consolidated financial statements include the accounts of the Company and its wholly owned subsidiaries. All significant intercompany balances and transactions have been eliminated in consolidation.

***Cash and Cash Equivalents***

The Company considers all highly liquid investments with maturities of three months or less from the date of purchase to be cash equivalents. Cash and cash equivalents at December 31, 2017 and 2016 consisted of cash and money market funds.

***Fair Value Measurements***

The Company's financial instruments consist principally of cash and cash equivalents, accounts receivable, accounts payable, and accrued liabilities. Fair value measurements are classified and disclosed in one of the following three categories:

Level 1 — Quoted prices in active markets for identical assets or liabilities.

Level 2 — Inputs other than Level 1 that are observable, either directly or indirectly, such as quoted prices for similar assets or liabilities; quoted prices in markets that are not active; or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.

Level 3 — Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

Financial instruments measured at fair value as of December 31, 2017 and 2016 are classified below based on the three fair value hierarchy tiers described above (in thousands):

| | | Fair Value Measurements at Reporting Date Using | | |
|---|---|---|---|---|
| | Balance | Level 1 | Level 2 | Level 3 |
| **December 31, 2017** | | | | |
| Cash and money market funds | $ 136,411 | $ 136,411 | $ — | $ — |
| **December 31, 2016** | | | | |
| Cash and money market funds | $ 142,086 | $ 142,086 | $ — | $ — |

The Company measures cash equivalents at fair value on a recurring basis. The fair value of cash equivalents is determined based on "Level 1" inputs, which consist of quoted prices in active markets for identical assets.

***Accounts Receivable***

Accounts receivable at December 31, 2017 and 2016 represent amounts due from two parties: (1) CUBRC, under the Company's subcontracts with respect to the National Institutes of Health's National Institute of Allergy and Infectious Diseases ("NIAID") division contract awarded for the development of TP-271 ("NIAID Contract") and the Biomedical Advanced Research and Development Authority ("BARDA"), an agency of the U.S. Department of Health and Human Services and under the Company's subaward under a separate grant from the NIAID ("NIAID Grant"); and (2) CARB-X. The Company's practice is to bill CUBRC and CARB-X the amounts for which the Company has been invoiced by third parties in the case of contract research or subcontractor costs or for internal costs incurred. Expenses directly associated with the Company's NIAID and BARDA Contracts, NIAID Grant and

CARB-X award that have been accrued at the end of the reporting period are not billed to the prime contractor until third-party invoices have been received or until internal costs have been paid. Unbilled accounts receivable, included in accounts receivable in the accompanying balance sheets, were $2.4 million and $0.4 million at December 31, 2017 and 2016, respectively.

***Property and Equipment, Net***

Property and equipment are stated at cost, less accumulated depreciation and amortization. Depreciation and amortization are recognized using the straight-line method over the estimated useful lives of the respective assets, which is generally three to five years. Leasehold improvements are amortized over the shorter of the lease term or the estimated useful economic lives of the related assets.

***Restricted Cash***

At December 31, 2017 and 2016, the Company had $199,000 in restricted cash deposits with a bank, of which $159,000 is collateral for a letter of credit issued to the landlord of the Company's leased facility. If the Company defaults on its rental obligations, $159,000 will be payable to the landlord. In addition, the Company has $40,000 in restricted cash to secure the Company's corporate credit card issued through the same bank.

***Revenue Recognition***

The Company's revenue has been derived from its subcontracts with CUBRC under the BARDA Contract, and the NIAID Contract, its subaward under the NIAID Grant and its cost reimbursement Sub-Award Agreement with the Trustees of Boston University, the administrator of the CARB-X program (Note 3). The Company recognizes revenue under these best-efforts, cost-reimbursable and cost-plus-fixed-fee subcontracts and subaward as the Company performs services under the subcontracts and subaward so long as a subcontract and subaward has been executed and the fees for these services are fixed or determinable, legally billable and reasonably assured of collection. Recognized amounts reflect the Company's partial performance under the subcontracts and subaward and equal direct and indirect costs incurred plus fixed fees, where applicable. The Company does not recognize revenue under these arrangements for amounts related to contract periods where funding is not yet committed as amounts above committed funding thresholds would not be considered fixed or determinable or reasonably assured of collection. Revenues and expenses under these arrangements are presented gross on the condensed consolidated statements of operations and comprehensive loss as the Company has determined it is the primary obligor under these arrangements relative to the research and development services it performs as lead technical expert.

Revenue under the Company's subcontracts under both the NIAID Contract and the BARDA Contract and under the CARB-X Aware are earned under a cost-plus-fixed-fee arrangement in which the Company is reimbursed for direct costs incurred plus allowable indirect costs and a fixed-fee earned. Billings under these arrangements are based on approved provisional indirect billing rates, which permit recovery of allowable fringe benefits, allowable overhead and general and administrative expenses and a fixed fee.

Revenue under the Company's subaward under the NIAID Grant was earned under a cost-reimbursable arrangement in which the Company was reimbursed for direct costs incurred plus allowable indirect costs. Billings under the NIAID Grant are based on approved provisional indirect billing rates, which permit recovery of fringe benefits and allowable general and administrative expenses.

***Research and Development Expenses***

Research and development costs are charged to expense as incurred and include, but are not limited to:

- personnel-related expenses, including salaries, benefits, and stock-based compensation expense;
- expenses incurred under agreements with contract research organizations, contract manufacturing organizations and consultants that provide preclinical, clinical, regulatory and manufacturing services;
- payments made under the Company's license agreement with Harvard University;
- the cost of acquiring, developing and manufacturing clinical trial materials and lab supplies;
- facility, depreciation and other expenses, which include direct and allocated expenses for rent, maintenance of the Company's facilities, insurance and other supplies; and
- costs associated with preclinical, regulatory and medical affair activities.

Costs for certain development activities, such as clinical trials, are recognized based on an evaluation of the progress to completion of specific tasks using data such as patient enrollment, clinical site activations, or information provided to the Company by its vendors on their actual costs incurred. Payments for these activities are based on the terms of the individual arrangements, which may differ from the pattern of costs incurred, and are reflected in the financial statements as prepaid or accrued research and development. In certain circumstances, the Company is required to make nonrefundable advance payments to vendors for goods or services that will be received in the future for use in research and development activities. In such circumstances, the nonrefundable advance payments are deferred and capitalized, even when there is no alternative future use for the research and development, until related goods or services are provided.

***Comprehensive Loss***

Comprehensive loss consists of net income or loss and changes in equity during a period from transactions and other events and circumstances generated from non-owner sources. The Company's net loss equals comprehensive loss for all periods presented.

***Income Taxes***

The Company uses the liability method of accounting for income taxes. Under this method, deferred tax assets and liabilities are determined based on the difference between the financial reporting and the tax reporting basis of assets and liabilities and are measured using the enacted tax rates and laws that are expected to be in effect when the differences are expected to reverse. The Company provides a valuation allowance against net deferred tax assets unless, based upon the available evidence, it is more likely than not that the deferred tax assets will be realized. The Company has evaluated available evidence and concluded that the Company may not realize the benefit of its deferred tax assets; therefore a valuation allowance has been established for the full amount of the deferred tax assets. The Company's practice is to recognize interest and/or penalties related to income tax matters in income tax expense.

The Tax Cuts and Jobs Act ("the Act") was enacted on December 22, 2017. The Act reduces the US federal corporate tax rate from 34% to 21%, requires companies to pay a one-time transition tax on earnings of certain foreign subsidiaries that were previously tax deferred and creates new taxes on certain foreign sourced earnings. On December 22, 2017, the Securities and Exchange Commission issued guidance under Staff Accounting Bulletin No. 118, Income Tax Accounting Implications of the Tax Cuts and Jobs Act ("SAB 118") directing taxpayers to consider the impact of the U.S. legislation as "provisional" when it does not have the necessary information available, prepared or analyzed (including computations) in reasonable detail to complete its accounting for the change in tax law.

At December 31, 2017, we have not completed our accounting for the tax effects of enactment of the Act; however, as described below, we have made a reasonable estimate of the effects on our existing deferred tax balances and the one-time transition tax. For the year ended December 31, 2017, we recognized no transition tax. In all cases, we will continue to make and refine our calculations as additional analysis is completed. In addition, our estimates may also be affected as we gain a more thorough understanding of the tax law.

***Stock-Based Compensation***

The Company determines stock-based compensation at the grant date using the Black-Scholes option pricing model to estimate fair value for employee equity awards. The Company recognizes the value of the award as an expense on a straight-line basis over the requisite service period using the estimated fair market value of the stock and accounts for forfeitures as they occur. For employee awards with performance conditions, the Company assesses whether the condition is probable of achievement, in which case, the fair value of the award is recognized over the requisite service period. The Company records stock-based compensation expense for payments issued to non-employees based on the fair value of the awards using the Black-Scholes option pricing model. Stock-based compensation payments issued to non-employees are revalued at each reporting period and as the equity instruments vest and are recognized as expense using the accelerated attribution method over the related service period.

***Going Concern Assessment***

Accounting Standards Update ("ASU") No. 2014-15, *Presentation of Financial Statements - Going Concern,* requires management to evaluate the company's ability to continue as a going concern one year beyond the filing date of the given financial statements. This evaluation requires management to perform two steps. First, management must evaluate whether there are conditions and events that raise substantial doubt about the entity's ability to continue as a going concern. Second, if management concludes that substantial doubt is raised, management is required to consider whether it has plans in place to alleviate that doubt. Disclosures in the notes to the financial statements are required if management concludes that substantial doubt exists or that its plans alleviate the substantial doubt that was raised.

Based on a detailed cash forecast incorporating current development activities and related spending plans, the Company expects its cash to last more than one year beyond the date that the financial statements were issued. Based on this analysis, no additional disclosures were required.

***Recent Accounting Pronouncements Issued***

In May 2014, the Financial Accounting Standard Board ("FASB") issued ASU No. 2014-09, *Revenue from Contracts with Customers (Topic 606)*, which supersedes all existing revenue recognition requirements, including most industry-specific guidance. The new standard requires a company to recognize revenue when it transfers goods or services to customers in an amount that reflects the consideration that the company expects to receive for those goods or services. In August 2015, the FASB issued ASU No. 2015-14, *Revenue from Contracts with Customers (Topic 606): Deferral of the Effective Date*, which delayed the effective date of the new standard from January 1, 2017 to January 1, 2018. The FASB also agreed to allow entities to choose to adopt the standard as of the original effective date. The FASB has subsequently issued ASU 2016-08, *Revenue from Contracts with Customers (Topic 606): Principal versus Agent Considerations (Reporting Revenue Gross versus Net)*; ASU 2016-10, *Revenue from Contracts with Customers (Topic 606): Identifying Performance Obligations and Licensing*; ASU 2016-12, *Revenue from Contracts with Customers (Topic 606): Narrow-Scope Improvements and Practical Expedients*; and ASU 2016-20, *Technical Corrections and Improvements to Topic 606, Revenue from Contracts with Customers*. The Company is in the process of completing its evaluation of the potential impact that these updates may have on its financial position, results of operations and cash flows, specifically the impact on its revenue recognized via its open contracts with the BARDA, NIAID and CARB-X. While its evaluation is not yet complete, the Company does not currently expect a significant change to its accounting for these contracts.

In February 2016, the FASB issued ASU No. 2016-02, *Leases (Topic 842)*. The new standard requires that all lessees recognize the assets and liabilities that arise from leases on the balance sheet and disclose qualitative and quantitative information about its leasing arrangements. The new standard will be effective for the Company on January 1, 2019. The Company is currently evaluating the potential impact that this standard may have on its financial position, results of operations and cash flows.

In March 2016, the FASB issued ASU No. 2016-09, *Improvements to Employee Share-Based Payment Accounting* ("ASU 2016-09"). ASU 2016-09 simplifies several aspects of the accounting for share-based payment transactions, including the income tax consequences, classification of awards as either equity or liabilities, forfeiture rates, and classification on the statement of cash flows. The new guidance is effective for fiscal years beginning after December 15, 2016, including interim periods within those annual reporting periods. The Company adopted ASU No. 2016-09 as of January 1, 2017. As a result of adopting ASU No. 2016-09, the Company elected to recognize share-based award forfeitures only as they occur rather than by applying an estimated forfeiture rate as previously required. ASU No. 2016-09 requires that this change be applied using a modified-retrospective transition method by means of a cumulative-effect adjustment to retained earnings as of the beginning of the fiscal year in which the guidance is adopted. The Company did not make an adjustment to retained earnings as the amount was immaterial to the financial statements.

In August 2016, the FASB issued ASU No. 2016-15, *Statement of Cash Flows (Topic 230): Classification of Certain Cash Receipts and Cash Payments* ("ASU 2016-15"). This new standard provides guidance to ensure consistency in how transactions are reflected in the statement of cash flows. ASU 2016-15 will be effective for the Company for annual periods beginning after December 15, 2017. The Company is currently evaluating the potential impact that this standard may have on its statements of cash flows.

In November 2016, the FASB issued ASU No. 2016-18, *Restricted Cash* ("ASU 2016-18"). ASU 2016-18 clarifies how entities should present restricted cash and restricted cash equivalents in the statement of cash flows. The guidance will be applied retrospectively and will be effective for the Company for annual and interim periods beginning after December 15, 2017. The Company is currently evaluating the potential impact that this standard may have on its financial position, statements of operations and cash flows.

In May 2017, the FASB issued ASU No. 2017-09, *Compensation - Stock Compensation (Topic 718): Scope of Modification Accounting* ("ASU 2017-09"). The new standard provides guidance about which changes to the terms or conditions of a share-based payment award require an entity to apply modification accounting in Topic 718. The new standard will be effective for the Company on January 1, 2018. The Company is currently evaluating the potential impact that this standard may have on its financial position, statements of operations and cash flows.

***Subsequent Events***

*Everest Medicines License Agreement*

In February 2018, the Company entered into a license agreement (the "License Agreement") with Everest Medicines Limited ("Everest Medicines "), whereby the Company granted Everest Medicines an exclusive license to develop and commercialize

eravacycline, for the treatment of complicated intra-abdominal infections and other indications, in mainland China, Taiwan, Hong Kong, Macau, South Korea and Singapore (the "Territory").

Under the terms of the License Agreement, the Company is eligible to receive from Everest Medicines an upfront cash payment of $7.0 million to be paid within 15 business days of the effective date of the License Agreement, and up to an aggregate of $16.5 million in clinical development and regulatory milestone payments and up to $20.0 million annually, provided that certain sales thresholds are met. There can be no guarantee that any such milestones or sales thresholds will in fact be met. The Company is obligated to make certain payments to Harvard University based on amounts received from Everest Medicines under the License Agreement pursuant to the existing license agreement by and between the Company and The President and Fellows of Harvard College, dated August 3, 2006, and as amended to date.

The Company will also be entitled to receive double-digit tiered royalties on sales in the Territory, if any, of products containing eravacycline. Royalties are payable with respect to each jurisdiction in the Territory until the latest to occur of: (i) the last-to-expire of specified patent rights in such jurisdiction in the Territory; (ii) expiration of marketing or regulatory exclusivity in such jurisdiction in the Territory; or (iii) ten (10) years after the first commercial sale of a product in such jurisdiction in the Territory. In addition, royalties payable under the License Agreement will be subject to reduction on account of generic competition and after patent expiry in a jurisdiction if required by applicable law, with any such reductions capped at certain percentages of the amounts otherwise payable during the applicable royalty payment period.

Under the terms and conditions of the License Agreement, Everest Medicines will be solely responsible for the development and commercialization of licensed products in the Territory.

*PDUFA Date*

In February 2018, the Company announced that the FDA had notified it that the FDA had completed its initial 60-day review of the NDA and August 28, 2018 was set as the PDUFA goal date for the FDA's completion of its review of the NDA for eravacycline for treatment of cIAI.

***Net Loss per Common Share***

Basic net loss per share is calculated by dividing the net loss by the weighted average number of shares of Common Stock outstanding for the period, without consideration for common stock equivalents. Diluted net loss per share is computed by dividing the net loss by the weighted average number of common share equivalents outstanding for the period determined using the treasury-stock method. For purposes of this calculation, warrants, stock options, and restricted stock units are considered to be common stock equivalents and are only included in the calculation of diluted net loss per share when their effect is dilutive.

The amounts in the table below were excluded from the calculation of diluted weighted-average shares outstanding, prior to the use of the treasury stock method, due to their anti-dilutive effect:

| | Year Ended December 31, | | |
|---|---|---|---|
| | **2017** | **2016** | **2015** |
| Warrants | - | 1,103 | 1,103 |
| Outstanding stock options | 5,997,794 | 4,066,411 | 3,833,806 |
| Unvested restricted stock units | 282,034 | 254,378 | 308,875 |
| Total | 6,279,828 | 4,321,892 | 4,143,784 |

**(3) Significant Agreements and Contracts**

***License Agreement***

In August 2006, the Company entered into a license agreement for certain intellectual property with Harvard University (the "University"). Under the license agreement, as of December 31, 2017, the Company has paid the University an aggregate of $6.1 million in upfront license fees and development milestone payments, and has issued 31,379 shares of common stock to the University.

For each product covered by the license agreement, the Company is obligated to make certain payments totaling up to approximately $15.1 million upon achievement of certain development and regulatory milestones and to pay additional royalties on net sales of such product. In January 2007 and April 2010, the Company and the University amended the license agreement to include certain additional intellectual property. The Company paid an additional $25,000 to the University with each amendment. In February

2011, the license agreement was further amended to include additional intellectual property in the license granted by the University without the payment of any additional consideration. The license agreement was further amended in December 2017 to change certain payments due to Harvard. A milestone payment of $1.8 million was made to Harvard in 2017 following submission of the MAA for eravacycline with the EMA.

***Government Grant and Contracts***

*BARDA Contract for Eravacycline*

The Company has received funding for its lead product candidate, eravacycline, under an award from to CUBRC from BARDA. In January 2012, BARDA awarded a five-year contract that provides for up to a total of $67.3 million in funding for the development, manufacturing and clinical evaluation of eravacycline for the treatment of disease caused by bacterial biothreat pathogens. The funding under the BARDA Contract is also being used for the development, manufacturing and clinical evaluation of eravacycline to treat certain infections caused by life-threatening multidrug-resistant bacteria.

In connection with the BARDA Contract, in February 2012, the Company entered into a cost-plus-fixed-fee subcontract with CUBRC which currently expires on December 31, 2018 under which the Company may receive funding of up to approximately $41.9 million, reflecting the portion of the BARDA Contract funding that may be paid to the Company for its activities.

Although the BARDA Contract and the Company's subcontract with CUBRC under the BARDA Contract have terms which currently expire on May 10, 2018, BARDA is entitled to terminate the project for convenience at any time, and is not obligated to provide continued funding beyond current-year amounts from Congressionally approved annual appropriations. To the extent that BARDA ceases to provide funding of the program to CUBRC, CUBRC has the right to cease providing funding to the Company. Committed funding from CUBRC under the Company's BARDA subcontract is up to $41.9 million through December 31, 2018, the current contract end date, as a result of the exercise of several options by BARDA under the BARDA Contract. Total funds of $35.7 million had been received by the Company through December 31, 2017 under this contract. During the years ended December 31, 2017, 2016 and 2015, the Company recognized revenue of $5.5 million, $2.9 million and $10.8 million, respectively, from the Company's subcontract under the BARDA Contract.

*NIAID Grant and Contract for TP-271*

The Company has received funding for its preclinical compound TP-271 under two awards to CUBRC from NIAID for the development, manufacturing, and clinical evaluation of TP-271 for respiratory diseases caused by biothreat and antibiotic-resistant public health pathogens, as well as bacterial pathogens associated with community-acquired bacterial pneumonia:

- the NIAID Grant awarded in July 2011 that provided up to a total of approximately $2.9 million over five years; and
- the NIAID Contract awarded in September 2011 that provides up to a total of approximately $35.8 million in funding over five years.

In connection with the NIAID Grant, in November 2011, CUBRC awarded the Company a no-fee subaward of approximately $0.9 million, reflecting the portion of the NIAID Grant funding that may be paid to the Company for its activities.

In connection with the NIAID Contract, in October 2011, the Company entered into a cost-plus-fixed-fee subcontract with CUBRC which currently expires on March 31, 2019 under which the Company may receive funding of up to approximately $16.9 million, reflecting the portion of the NIAID Contract funding that may be paid to the Company for its activities.

Although the NIAID Contract and the Company's subcontract with CUBRC under the NIAID Contract have terms which currently expire on March 31, 2019, and the Company's subaward under the NIAID Grant has a term which expired on May 31, 2017, NIAID is entitled to terminate the project for convenience at any time, and is not obligated to provide continued funding beyond the respective expiration dates. To the extent that NIAID ceases to provide funding of the programs to CUBRC, CUBRC has the right to cease providing funding to the Company. As of December 31, 2017, committed funding from CUBRC under the Company's subcontract with respect to the NIAID Contract is $16.9 million, of which $13.2 million had been received through December 31, 2017. Through December 31, 2017, the Company had received all committed funding of $0.9 million from CUBRC under the Company's subaward with respect to the NIAID Grant.

During the years ended December 31, 2017, 2016 and 2015, the Company recognized revenue of $3.5 million, $2.2 million, and $0.8 million, respectively, from the Company's subcontract under the NIAID Contract. During the years ended December 31, 2017, 2016 and 2015, the Company recognized revenue of $9,000, $102,000 and $157,000, respectively, from the Company's subaward under the NIAID Grant.

*CARB-X Award for TP-6076*

In March 2017, CARB-X selected the Company to receive up to $4.0 million in research funding over eighteen months for TP-6076. In connection with this funding, the Company entered into a cost reimbursement Sub-Award Agreement (the "Sub-Award Agreement") with the Trustees of Boston University, the administrator of the program. The Company began recognizing revenue from the Sub-Award Agreement in April 2017. During the year ended December 31, 2017, the Company recognized revenue of $0.7 million under this Sub-Award Agreement. This Sub-Award Agreement will fund certain activities through the end of 2018. This Sub-Award Agreement can be terminated for convenience at any time, subject to 30 days prior written notice.

**(4) Property and Equipment**

Property and equipment at December 31, 2017 and 2016 consisted of the following (in thousands):

| | Estimated Useful Life In Years | December 31, 2017 | December 31, 2016 |
|---|---|---|---|
| Laboratory equipment | 5 | $ 3,101 | $ 2,358 |
| Furniture and fixtures | 5 | 509 | 509 |
| Office and computer equipment | 3 | 208 | 232 |
| Leasehold improvements | | 923 | 915 |
| Property and equipment, gross | | 4,741 | 4,014 |
| Less accumulated depreciation and amortization | | (3,346) | (2,960) |
| Property and equipment, net | | $ 1,395 | $ 1,054 |

Depreciation and amortization expense for the years ended December 31, 2017, 2016 and 2015 was $431,000, $282,000 and $193,000, respectively.

**(5) Accrued Expenses**

Accrued expenses at December 31, 2017 and 2016 consisted of the following (in thousands):

| | December 31, 2017 | December 31, 2016 |
|---|---|---|
| Salaries and benefits | $ 4,137 | $ 2,498 |
| Clinical trial related | 3,401 | 1,129 |
| Drug supply and development | 2,298 | 2,698 |
| Professional fees | 1,911 | 965 |
| Other | 812 | 395 |
| Total | $ 12,559 | $ 7,685 |

**(6) Stockholders' Equity**

*2015 Follow-on Public Offering*

In March 2015, the Company sold 4,945,000 shares of common stock in a follow-on public offering at a price to the public of $35.00 per share, resulting in net proceeds to the Company of $162.2 million after deducting underwriting discounts and commissions of $10.4 million and offering costs of $0.5 million.

In January 2017, the Company entered into a Controlled Equity Offering Sales Agreement (the "Sales Agreement"), with Cantor Fitzgerald & Co. as sales agent ("Cantor"). In July 2017, the Company entered into an amendment to the Sales Agreement to increase the maximum aggregate offering price of the shares of common stock that it may issue and sell from time to time under the Sales Agreement from $40,000,000 to $80,000,000.

Under the Sales Agreement, as amended (the "Amended Sales Agreement"), Cantor may sell shares of the Company's common stock by methods deemed to be an "at-the-market" offering as defined in Rule 415 promulgated under the Securities Act of 1933, as amended, including sales made directly on The NASDAQ Global Select Market or on any other existing trading market for the Company's common stock.

The Company is not obligated to make any sales of shares of its common stock under the Amended Sales Agreement. The Company or Cantor may suspend or terminate the offering of shares of the Company's common stock upon notice to the other party and subject to other conditions. The Company pays Cantor a commission rate equal to 3.0% of the gross proceeds per share sold.

As of December 31, 2017, the Company had sold an aggregate of 4,157,873 shares of common stock under the Sales Agreement, at an average selling price of approximately $7.78 per share for aggregate gross proceeds of $32.4 million and net proceeds of $31.1 million after deducting the sales commissions and offering expenses. As of March 4, 2018, $47.6 million of common stock remained available to be sold under the Amended Sales Agreement, subject to certain conditions specified therein.

On August 2, 2017, the Company sold 10,000,000 shares of common stock in an underwritten public offering at an offering price to the public of $6.50 per share, resulting in net proceeds to the Company of $60.7 million after deducting underwriting discounts and commissions of $3.9 million and offering costs of $0.4 million. In connection with the offering, the Company granted the underwriters an option to purchase up to an additional 1,500,000 shares on the same terms and conditions as the offering, pursuant to which the underwriters exercised an option to purchase 107,000 additional shares on August 25, 2017, resulting in additional net proceeds to the Company of approximately $0.7 million after deducting underwriting discounts and commissions.

**(7) Stock-based Compensation**

In February 2013, the Company's board of directors and stockholders approved, effective upon the closing of the IPO, the 2013 Stock Incentive Plan (the "2013 Plan"). Under the 2013 Plan, the Company may grant incentive stock options, nonstatutory stock options, stock appreciation rights, restricted stock, restricted stock units and other stock-based awards for the purchase of that number of shares of Common Stock equal to the sum of (i) 1,688,777 shares of Common Stock, (ii) 258,265 shares of Common Stock that were reserved for issuance under the 2006 Plan that remained available for issuance under the 2006 Plan upon the closing of the IPO, (iii) any shares of Common Stock subject to awards under the 2006 Plan which awards expire, terminate or are otherwise surrendered, canceled, forfeited or repurchased by the Company without having been fully exercised or resulting in any Common Stock being issued. In addition, the number of shares of Common Stock that may be issued under the 2013 Plan is subject to automatic annual increases, to be added on January 1 of each year from January 1, 2014 through and including January 1, 2023, equal to the number of shares that is the lesser of (a) 3,000,000, (b) 4% of the then outstanding shares of Common Stock or (c) an amount determined by the Company's board of directors. In January 2015, the number of shares authorized for issuance under the 2013 Plan increased by 1,232,232 shares. In January 2016, the number of shares authorized for issuance under the 2013 Plan increased by 1,463,391 shares. In January 2017, the number of shares authorized for issuance under the 2013 Plan increased by 1,477,677 shares. As of December 31, 2017, 890,011 shares were available for future issuance under the 2013 Plan. In January 2018, the number of shares authorized for issuance under the 2013 Plan increased by 2,058,300 shares.

Terms of stock award agreements, including vesting requirements, are determined by the board of directors, subject to the provisions of the 2013 Plan. Options granted by the Company typically vest over a four year period. Certain of the options are subject to acceleration of vesting in the event of certain change of control transactions. The options are exercisable from the date of grant for a period of ten years. For options granted prior to the Company's IPO, the exercise price equaled the estimated fair value of the Common Stock as determined by the board of directors on the date of grant. For options granted subsequent to the Company's IPO, the exercise price equaled the closing price of the Company's stock on the NASDAQ Global Select Market on the date of grant.

Stock option activity at December 31, 2017 and changes during the year then ended are presented in the table and narrative below (in thousands, except share and per share data):

| | Shares | Weighted-Average Exercise Price | Weighted-Average Remaining Contractual Term (years) | Aggregate Intrinsic Value |
|---|---|---|---|---|
| Options outstanding at December 31, 2016 | 4,066,411 | $ 18.42 | 7.62 | $ 687 |
| Granted | 2,532,250 | 4.50 | | |
| Exercised | (88,319) | 3.27 | | |
| Canceled | (512,548) | 11.84 | | |
| Options outstanding at December 31, 2017 | 5,997,794 | $ 13.33 | 7.14 | $ 6,065 |
| Options exercisable at December 31, 2017 | 3,142,636 | $ 16.41 | 5.70 | $ 2,274 |

The aggregate intrinsic value in the table above represents the difference between the Company's closing common stock price on the last trading day during the year ended December 31, 2017 and the exercise price of the options, multiplied by the number of in-the-money options. The total intrinsic value of options exercised in the years ended December 31, 2017, 2016, and 2015 was $0.2 million, $0.3 million and $27.0 million, respectively. As of December 31, 2017, there was $16.1 million of total unrecognized stock-based compensation cost related to employee and non-employee unvested stock options granted under the 2006 Plan and the 2013 Plan. The Company expects to recognize that cost over a remaining weighted-average period of 2.5 years.

Since the Company completed its IPO on March 25, 2013, it has not had sufficient historical data to support a calculation of volatility and expected life. As such, the Company has used a weighted-average volatility considering the Company's own volatility and the volatilities of a representative group of publicly traded companies. For purposes of identifying similar entities, the Company selected a group of publicly traded life science/biotechnology companies based on their disease focus, stage of development, number of compounds in clinical trials and number of years as a publicly-traded company. The risk-free interest rate is based on the U.S. Treasury yield curve in effect at the time of grant, commensurate with the expected life assumption. The expected life of stock options granted represents the weighted-average period of time that stock options granted are expected to be outstanding determined using the simplified method for employee grants. For non-employee grants, the expected life is equal to the remaining contractual term. The expected life is applied to the stock option grant group as a whole, as the Company does not expect substantially different exercise or post-vesting termination behavior among its employee population.

The Company estimates the fair value of each employee and director stock option award on the grant date using the Black-Scholes option-pricing model based on the following assumptions:

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2017 | 2016 | 2015 |
| Volatility factor | 89.24%-90.56% | 85.77%-87.82% | 56.49%-85.34% |
| Expected life (in years) | 5.31-6.11 | 5.31-6.21 | 5.31-6.11 |
| Risk-free interest rate | 1.78%-2.18% | 1.25%-2.10% | 1.35%-1.94% |
| Dividend yield | 0% | 0% | 0% |

Compensation cost for stock options and restricted stock units granted to employees is based on the estimated grant-date fair value and is recognized over the vesting period of the applicable option on a straight-line basis. Stock-based compensation expense related to stock options and restricted stock units granted to employees was $12.0 million, $13.1 million, and $11.6 million during the years ended December 31, 2017, 2016, and 2015, respectively.

Using the Black-Scholes option-pricing model, the weighted-average grant date fair values of options granted to employees for the years ended December 31, 2017, 2016 and 2015 was $4.50, $7.53 and $22.78, respectively.

Stock-based compensation expense recognized in the Company's consolidated statements of operations during the periods presented was as follows (in thousands):

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2017 | 2016 | 2015 |
| Research and development | $ 5,768 | $ 6,661 | $ 5,906 |
| General and administrative | 6,195 | 6,484 | 5,710 |
| Total (includes employee and non-employee stock compensation) | $ 11,963 | $ 13,145 | $ 11,616 |

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2017 | 2016 | 2015 |
| Stock options | $ 11,156 | $ 11,230 | $ 10,865 |
| Restricted stock units | 686 | 1,757 | 596 |
| Employee stock purchase plan | 121 | 158 | 155 |
| Total (includes employee and non-employee stock compensation) | $ 11,963 | $ 13,145 | $ 11,616 |

***Restricted Stock Units***

In January 2016, the Company granted additional restricted stock units to employees. These restricted stock units vest in annual increments over three years, subject to continued employment with the Company and had a grant date fair value of $8.47 per share, which was the closing price of the Company's common stock on the date of grant.

In January 2017, the Company issued restricted stock units with service and performance conditions to certain employees, none of which vested during the twelve months ended December 31, 2017. Vesting of these awards is contingent on the occurrence of certain milestone events and fulfillment of any remaining service condition. As a result, the related compensation cost is recognized as an expense when achievement of the milestone is considered probable over the remaining requisite service period.

The following table summarizes the restricted stock activity for the year ended December 31, 2017:

| | Shares | Grant Date Fair Value |
|---|---|---|
| Unvested at December 31, 2016 | 254,378 | $ 8.47 |
| Granted | 175,000 | 3.83 |
| Cancelled | (62,572) | 6.25 |
| Vested/Released | (84,772) | 8.47 |
| Unvested at December 31, 2017 | 282,034 | $ 6.09 |

As of December 31, 2017, there was $1.0 million of total unrecognized stock-based compensation expense related to restricted stock units granted under the Plan. The expense is expected to be recognized over a weighted-average period of 1.6 years.

**(8) Employee Stock Purchase Plan**

On February 27, 2014, upon the recommendation of the Company's compensation committee, the Company's board of directors adopted, subject to stockholder approval, the 2014 Employee Stock Purchase Plan (the "ESPP") pursuant to which the Company may sell up to an aggregate of 300,000 shares of Common Stock. The ESPP was approved by the Company's stockholders on June 12, 2014. The ESPP allows eligible employees to purchase common stock at a price per share equal to 85% of the lower of the fair market value of the common stock at the beginning or end of each period during the term of the ESPP. The offering periods are six months each from May to November and from November to May of each calendar year. Pursuant to the ESPP, the Company sold a total of 77,604 shares of common stock during the year ended December 31, 2017 under the ESPP at purchase prices of $3.43, and $5.10, respectively, which represented 85% of the closing price of the Company's common stock on May 12, 2017, and November 14, 2017, respectively. Pursuant to the ESPP, the Company sold a total of 58,702 shares of common stock during the year ended December 31, 2016 under the ESPP at purchase prices of $2.95, and $3.32, respectively, which represented 85% of the closing price of the Company's common stock on May 13, 2016, and November 14, 2016, respectively. Pursuant to the ESPP, the Company sold a total of 16,422 shares of common stock during the year ended December 31, 2015 under the ESPP at purchase prices of $19.29 and $9.30, respectively, which represented 85% of the closing price of the Company's common stock on May 14, 2015 and November 14, 2015, respectively. The Company records stock-based compensation expense under the ESPP based on the fair value of the purchase rights using the Black-Scholes option pricing model. The total stock-based compensation expense recorded as a result of the ESPP was $121,000, $158,000, and $156,000 during the years ended December 31, 2017, 2016 and 2015, respectively.

**(9) Income Taxes**

The Company accounts for income taxes under ASC 740, *Accounting for Income Taxes*. Deferred income tax assets and liabilities are determined based upon differences between financial reporting and tax bases of assets and liabilities and are measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse.

Loss before income tax (benefit) provision consists of the following (in thousands):

| | Year ended December 31, | | |
|---|---|---|---|
| | 2017 | 2016 | 2015 |
| United States | $ (94,748) | $ (62,536) | $ (64,037) |
| Foreign | (20,004) | (14,944) | (19,152) |
| Total loss before income taxes | $ (114,752) | $ (77,480) | $ (83,189) |

For the years ended December 31, 2017, 2016 and 2015 the Company did not have a current or deferred income tax expense or benefit.

A reconciliation of the Federal statutory tax rate of 34% to the Company's effective income tax rate follows:

| | Year ended December 31, | | |
|---|---|---|---|
| | 2017 | 2016 | 2015 |
| Statutory tax rate | (34.00)% | (34.00)% | (34.00)% |
| State taxes, net of Federal benefits | (4.37)% | (4.19)% | (4.02)% |
| Permanent differences | 1.18% | 1.19% | 0.71% |
| Credits | (0.96)% | (1.47)% | (1.65)% |
| Change in valuation allowance | (11.04)% | 29.78% | 30.74% |
| Foreign rate differential | 5.93% | 6.56% | 7.03% |
| Federal Rate Change - Tax Reform | 43.26% | — | — |
| Other | — | 2.13% | 1.19% |
| Effective tax rate | —% | —% | —% |

On December 22, 2017, the Tax Cuts and Jobs Act ("the Act") was enacted in the United States. The Act reduces the U.S. federal corporate tax rate from 34% to 21%, requires companies to pay a one-time transition tax on earnings of certain foreign subsidiaries that were previously tax deferred and creates new taxes on certain foreign sourced earnings. At December 31, 2017, we have not completed our accounting for the tax effects of enactment of the Act, including the effects on our existing deferred tax balances and the one-time transition tax. For the year ended December 31, 2017, we recognized no transition tax and have not recorded any additional taxes on the outside basis difference of our foreign subsidiary as our investment in the foreign subsidiary is essentially permanent in duration. Determining the amount of unrecognized deferred tax liability is not practicable. We are still in the process of analyzing the impact of the Act on our indefinite reinvestment assertion.

As a result of the Act, we remeasured certain deferred tax assets and liabilities based on the rates at which they are anticipated to reverse in the future, which is generally 21%. This resulted in a decrease to our gross deferred tax assets and a corresponding decrease in our valuation allowance of in the amount of $49.7 million.

Any items reported are done so using provisional amounts until the initial accounting required by the Act is complete. Additional time and resources are needed to ensure the correct implementation of the Act.

As of December 31, 2017 the Company had federal net operating loss carryforwards of approximately $384.7 million and state net operating loss carryforwards of $350.5 million, which are available to reduce future taxable income. The Company adopted ASU 2016-09, *Improvements to Employee Share-Based Payment Accounting*, during the quarter ended March 31, 2017, upon which the net operating loss carryforward deferred tax assets was increased by the excess tax benefits of $10.5 million (tax-effected) with a corresponding increase to the Company's valuation allowance.

The Company also had federal tax credits of $7.0 million and state tax credits of $2.6 million, which may be used to offset future tax liabilities. The net operating loss (NOL) and tax credit carryforwards will expire at various dates through 2037. The NOL and tax credit carryforwards are subject to review and possible adjustment by the Internal Revenue Service and state tax authorities. Net operating loss and tax credit carryforwards may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant shareholders over a three-year period in excess of 50%, as defined under Sections 382 and 383 of the Internal Revenue Code, respectively, as well as similar state provisions. This could limit the amount of tax attributes that can be utilized annually to offset future taxable income or tax liabilities. The amount of the annual limitation is determined based on the value of the Company immediately prior to the ownership change. Subsequent ownership changes may further affect the limitation in future years. The Company has not, as yet, conducted a study of research and development ("R&D") credit carryforwards. This study may result in an adjustment to the Company's R&D credit carryforwards.

The principal components of the Company's deferred tax assets are as follows (in thousands):

| | Year ended December 31, | |
|---|---|---|
| | 2017 | 2016 |
| Deferred tax assets: | | |
| Net operating loss carry forwards | $ 102,942 | $ 106,560 |
| Equity-based compensation | 7,073 | 6,937 |
| Other temporary differences | 1,169 | 1,235 |
| Research and development credit and carry forwards | 9,079 | 7,682 |
| Deferred tax assets | 120,263 | 122,414 |
| Less valuation allowance | (120,263) | (122,414) |
| Net deferred tax assets | $ — | $ — |

ASC 740 requires a valuation allowance to reduce the deferred tax assets reported, if based on the weight of available evidence, it is more likely than not that some portion or all of the deferred tax assets will not be realized. After consideration of all the evidence, both positive and negative, the Company has recorded a valuation allowance against its deferred tax assets at December 31, 2017 and 2016, respectively, because the Company's management has determined that is it more likely than not that these assets will not be realized. The $2.2 million decrease in the valuation allowance in 2017 primarily relates to the federal rate reduction from 34% to 21% as a result of the Tax Act, partially offset by the net loss incurred by the Company in 2017 and the impact of the adoption of ASU 2016-09.

ASC 740 clarifies the accounting for uncertainty in income taxes recognized in an enterprise's financial statement by prescribing the minimum recognition threshold and measurement of a tax position taken or expected to be taken in a tax return. The Company had gross tax-effected unrecognized tax benefits of $1.1 million and $1.0 million at December 31, 2017 and 2016, respectively. Unrecognized tax benefits represent tax positions for which reserves have been established. A full valuation allowance has been provided against the Company's deferred tax assets, so that the effect of any unrecognized tax benefits would simply be to reduce the gross amount of the deferred tax asset and the corresponding valuation allowance. The Company anticipates that the amount of unrecognized tax benefits recorded will not change in the next twelve months.

As of December 31, 2017 and 2016, the Company had no accrued interest or penalties related to uncertain tax positions.

The aggregate changes in gross unrecognized tax benefits during the years ended December 31, 2017, 2016, and 2015 were as follows (in thousands):

| | Year ended December 31, | | |
|---|---|---|---|
| | 2017 | 2016 | 2015 |
| Balance at beginning of year | $ 967 | $ 822 | — |
| Increases for tax positions taken during current period | 152 | 145 | 249 |
| Increases for tax positions taken in prior periods | — | — | 573 |
| Decreases for tax positions taken during current period | (12) | — | — |
| Decreases for tax positions taken in prior periods | — | — | — |
| Balance at end of year | $ 1,107 | $ 967 | $ 822 |

The Company is currently open to examination under the statute of limitations by the Internal Revenue Service and state jurisdictions for the tax years ended 2014 through 2016. Carryforward tax attributes generated in years past may still be adjusted upon future examination if they have or will be used in a future period. The Company is currently not under examination by the Internal Revenue Service or any other jurisdictions for any tax years.

**(10) Commitments and Contingencies**

***Lease Commitments***

On March 24, 2015, the Company amended its existing operating lease to expand its existing premises by an additional 13,711 square feet of office and laboratory space for a total of 29,610 square feet. The effective date of this amendment was April 1,

2015. On March 31, 2015, the Company canceled an existing sublease entered into in September 2014 covering 15,174 square feet of office and laboratory space.

On June 18, 2015, the Company further amended its existing operating lease to expand its leased premises by an additional 7,828 square feet of office and laboratory space for a total of 37,438 square feet. The lease for the additional office and laboratory space was effective as of August 1, 2015. In connection with the amendment, the lease term was extended from November 30, 2016 to November 30, 2019.

In the third quarter of 2016, the Company entered into a sublease with respect to a portion of its principal facilities with an unrelated third party. The term of the sublease expires in November 2019, with the sublessee obligated to pay rent to the Company that approximates the rent the Company is currently paying to its landlord with respect to such portion of its facility.

As of December 31, 2017, the aggregate minimum future rent payments under the lease agreement, net of the sublease agreement, are as follows (in thousands):

| | December 31, 2017 |
|---|---|
| 2018 | 1,752 |
| 2019 | 1,650 |
| Total minimum lease payments | $ 3,402 |

The Company recorded $1.4 million, $1.6 million and $1.7 million in rent expense for the years ended December 31, 2017, 2016 and 2015, respectively.

***Litigation***

In January 2016 and March 2016, two securities class action lawsuits were filed against the Company, the Company's chief executive officer, the Company's former chief operating officer and the Company's former chief financial officer, in the United States District Court for the District of Massachusetts. In May 2016, the court consolidated the two lawsuits and appointed lead plaintiffs and lead counsel. The lead plaintiffs filed a consolidated amended complaint in July 2016 and filed a second consolidated amended complaint in August 2016. The second amended complaint was brought on behalf of an alleged class of those who purchased the Company's common stock between March 5, 2015 and September 8, 2015, and alleged claims arising under Sections 10 and 20 of the Exchange Act of 2934, as amended. The complaint generally alleged that the defendants violated the federal securities laws by, among other things, making material misstatements or omissions concerning IGNITE2. The complaint sought, among other relief, unspecified compensatory damages, attorneys' fees and costs. In October 2016, the Company filed a motion to dismiss the second amended complaint in its entirety, which plaintiffs opposed. The Company's motion to dismiss was granted by the United States District Court for the District of Massachusetts in May 2017. In July 2017 plaintiffs appealed this decision to the United States Court of Appeals for the First Circuit, or the First Circuit. In November 2017 plaintiffs withdrew their appeal to the First Circuit.

**(11) Employee Benefit Plan**

In 2007, the Company established the Tetraphase Pharmaceuticals, Inc. 401(k) Plan (the "401(k) Plan") for its employees, which is designed to be qualified under Section 401(k) of the Internal Revenue Code. Eligible employees are permitted to contribute to the 401(k) Plan within statutory and 401(k) Plan limits. During 2014, the Company began to make matching contributions of 50% of the first 6% of employee contributions. The Company made matching contributions of $354,000, $311,000, and $261,000 for the years ended December 31, 2017, 2016, and 2015, respectively.

**(12) Quarterly Results (Unaudited)**

| | Three Months Ended | | | |
|---|---|---|---|---|
| | March 31, 2017 | June 30, 2017 | September 30, 2017 | December 31, 2017 |
| | (in thousands, except per share data) (unaudited) | | | |
| Revenue | $ 1,485 | $ 1,586 | $ 4,067 | $ 2,528 |
| Operating expenses | 31,080 | 33,578 | 34,377 | 26,346 |
| Loss from operations | (29,595) | (31,992) | (30,310) | (23,818) |
| Other income (expense), net | 137 | 181 | 302 | 343 |
| Net loss | $ (29,458) | $ (31,811) | $ (30,008) | $ (23,475) |
| Net loss per share—basic and diluted | $ (0.79) | $ (0.83) | $ (0.63) | $ (0.46) |

| | Three Months Ended | | | |
|---|---|---|---|---|
| | March 31, 2016 | June 30, 2016 | September 30, 2016 | December 31, 2016 |
| | (in thousands, except per share data) (unaudited) | | | |
| Revenue | $ 1,962 | $ 1,243 | $ 850 | $ 1,090 |
| Operating expenses | 18,776 | 18,505 | 22,048 | 23,646 |
| Loss from operations | (16,814) | (17,262) | (21,198) | (22,556) |
| Other expense, net | 73 | 94 | 88 | 95 |
| Net loss | $ (16,741) | $ (17,168) | $ (21,110) | $ (22,461) |
| Net loss per share—basic and diluted | $ (0.46) | $ (0.47) | $ (0.58) | $ (0.61) |

## ITEM 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

None.

## ITEM 9A. Controls and Procedures

**Evaluation of Disclosure Controls and Procedures**

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2017. In designing and evaluating our disclosure controls and procedures, management recognized that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and our management necessarily applied its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on this evaluation, our Chief Executive Officer and Chief Financial Officer concluded that as of December 31, 2017, our disclosure controls and procedures were (1) designed to ensure that material information relating to us is made known to our management including our principal executive officer and principal financial officer by others, particularly during the period in which this Annual Report on Form 10-K was prepared and (2) effective, in that they provide reasonable assurance that information required to be disclosed by us in the reports we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms.

The certifications of our principal executive officer and principal financial officer attached as Exhibits 31.1 and 31.2 to this report include, in paragraph 4 of such certifications, information concerning our disclosure controls and procedures and internal controls over financial reporting.

**Internal Control Over Financial Reporting**

***(a) Management's Report on Internal Control Over Financial Reporting***

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is defined in Rules 13a-15(f) and 15d-15(f) promulgated under the Exchange Act as a process designed by, or under the supervision of, the company's principal executive and principal financial officers and effected by the

company's board of directors, management and other personnel, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles and includes those policies and procedures that:

- Pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of the assets of the company;
- Provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and
- Provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Therefore, even those systems determined to be effective can provide only reasonable assurance with respect to financial statement preparation and presentation. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2017. In making this assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in *Internal Control—Integrated Framework* (2013 framework) (COSO). Based on its assessment, management believes that, as of December 31, 2017, our internal control over financial reporting is effective at the reasonable assurance level.

Ernst and Young LLP, our independent registered public accounting firm has audited the consolidated financial statements included in this Annual Report on Form 10-K and, as part of the audit, has issued a report on the effectiveness of our internal control over financial reporting as of December 31, 2017, which report is included herein.

*(b) Report of Independent Registered Public Accounting Firm on Internal Control over Financial Reporting*

**Report of Independent Registered Public Accounting Firm**

To the Stockholders and the Board of Directors of Tetraphase Pharmaceuticals, Inc.

**Opinion on Internal Control over Financial Reporting**

We have audited Tetraphase Pharmaceuticals, Inc.'s internal control over financial reporting as of December 31, 2017, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (the COSO criteria). In our opinion, Tetraphase Pharmaceuticals, Inc. (the Company) maintained, in all material respects, effective internal control over financial reporting as of December 31, 2017, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated balance sheets of the Company as of December 31, 2017 and 2016, the related consolidated statements of operations and comprehensive loss, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2017, and the related notes and our report dated March 6, 2018 expressed an unqualified opinion thereon.

**Basis for Opinion**

The Company's management is responsible for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Report on Internal Control Over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects.

Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

**Definition and Limitations of Internal Control Over Financial Reporting**

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ Ernst & Young LLP

Boston, Massachusetts
March 6, 2018

***(c) Changes in Internal Control Over Financial Accounting***

There were no changes in our internal control over financial reporting that occurred during the quarter ended December 31, 2017 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

**ITEM 9B. Other Information**

None.

## PART III

### ITEM 10. Directors, Executive Officers and Corporate Governance

The information required by this Item 10 will be contained in the sections entitled "Election of Directors" and "Section 16(a) Beneficial Ownership Reporting Compliance" appearing in the definitive proxy statement we will file in connection with our 2018 Annual Meeting of Stockholders and is incorporated by reference herein. The information required by this item concerning our code of ethics is set forth in the section entitled "Code of Business Conduct and Ethics" appearing in the definitive proxy statement we will file in connection with our 2018 Annual Meeting of Stockholders and is incorporated by reference herein. The information required by this item relating to executive officers is set forth in the section entitled "Executive Officers" appearing in the definitive proxy statement we will file in connection with our 2018 Annual Meeting of Stockholders and is incorporated by reference herein.

### ITEM 11. Executive Compensation

The information required by this Item 11 will be contained in the sections entitled "Executive and Director Compensation," "Compensation Committee Interlocks and Insider Participation" and "Compensation Committee Report" appearing in the definitive proxy statement we will file in connection with our 2018 Annual Meeting of Stockholders and is incorporated by reference herein.

### ITEM 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

The information required by this Item 12 will be contained in the sections entitled "Ownership of Our Common Stock" and "Executive and Director Compensation—Equity Compensation Plan Information" appearing in the definitive proxy statement we will file in connection with our 2018 Annual Meeting of Stockholders and is incorporated by reference herein.

### ITEM 13. Certain Relationships and Related Person Transactions, and Director Independence

The information required by this Item 13 will be contained in the sections entitled "Certain Relationships and Related Person Transactions" appearing in the definitive proxy statement we will file in connection with our 2018 Annual Meeting of Stockholders and is incorporated by reference herein.

### ITEM 14. Principal Accounting Fees and Services

The information required by this Item 14 will be contained in the section entitled "Corporate Governance—Principal Accountant Fees and Services" appearing in the definitive proxy statement we will file in connection with our 2018 Annual Meeting of Stockholders and is incorporated by reference herein.

## PART IV

### ITEM 15. Exhibits and Financial Statement Schedules

(a) Documents filed as part of Form 10-K.

(1) Financial Statements

Report of Independent Registered Public Accounting Firm

Consolidated Balance Sheets

Consolidated Statements of Operations and Comprehensive Loss

Consolidated Statements of Convertible Preferred Stock and Stockholders' Equity (Deficit)

Consolidated Statements of Cash Flows

Notes to Consolidated Financial Statements

(2) Schedules

Schedules have been omitted as all required information has been disclosed in the financial statements and related footnotes.

(3) Exhibits

The Exhibits listed in the Exhibit Index are filed as a part of this Form 10-K.

### ITEM 16. Form 10-K Summary

None.

**EXHIBIT INDEX**

| Exhibit Number | Description | Incorporated by Reference from | | | |
|---|---|---|---|---|---|
| | | Registrant's Form | File No. | Date Filed with the SEC | Exhibit Number |
| 3.1 | Restated Certificate of Incorporation of the Registrant | 10-Q | 001-35837 | 5/13/13 | 3.1 |
| 3.2 | Amended and Restated Bylaws of the Registrant | 10-Q | 001-35837 | 5/13/13 | 3.2 |
| 4.1 | Specimen certificate evidencing shares of common stock | S-1/A | 333-186574 | 3/5/13 | 4.1 |
| 10.1# | 2006 Stock Incentive Plan, as amended | S-1 | 333-186574 | 2/11/13 | 10.5 |
| 10.2# | Form of Incentive Stock Option Agreement under 2006 Stock Incentive Plan | S-1 | 333-186574 | 2/11/13 | 10.6 |
| 10.3# | Form of Nonstatutory Stock Option Agreement under 2006 Stock Incentive Plan | S-1 | 333-186574 | 2/11/13 | 10.7 |
| 10.4# | 2013 Stock Incentive Plan | S-1/A | 333-186574 | 3/5/13 | 10.8 |
| 10.5# | Form of Incentive Stock Option Agreement under 2013 Stock Incentive Plan | S-1/A | 333-186574 | 3/5/13 | 10.9 |
| 10.6# | Form of Nonstatutory Stock Option Agreement under 2013 Stock Incentive Plan | S-1/A | 333-186574 | 3/5/13 | 10.10 |
| 10.7# | Form of Restricted Stock Agreement under 2013 Incentive Plan | 10-K | 001-35837 | 3/13/17 | 10.7 |
| 10.8# | 2014 Employee Stock Purchase Plan | 10-Q | 001-35837 | 8/12/14 | 10.1 |
| 10.9# | Form of Nonstatutory Option Agreement for Inducement Grants | 10-Q | 001-35837 | 5/7/2015 | 10.3 |
| 10.10# | Offer letter, dated as of December 4, 2007, by and between the Registrant and Guy Macdonald, as amended | S-1 | 333-186574 | 2/11/13 | 10.11 |
| 10.11# | Second Amendment to Offer Letter, dated as of March 5, 2014, by and between the Registrant and Guy Macdonald | 10-Q | 001-35837 | 5/12/14 | 10.2 |
| 10.12# | Offer letter, dated as of June 11, 2015, by and between the Registrant and Jacques Dumas, as amended | 10-K | 001-35837 | 3/13/17 | 10.12 |
| 10.13#* | Offer letter, dated as of December 27, 2017, by and between the Registrant and Larry Tsai | | | | |
| 10.14# | Offer Letter, dated September 21, 2017, by and between the Registrant and Kamalam Unninayar | 10-Q | 001-35837 | 11/1/17 | 10.2 |
| 10.15# | Offer letter, dated as of February 16, 2015, by and between the Registrant and Maria Stahl | 10-Q | 001-35837 | 5/7/15 | 10.2 |

| Exhibit Number | Description | Registrant's Form | Incorporated by Reference from File No. | Date Filed with the SEC | Exhibit Number |
|---|---|---|---|---|---|
| 10.16# | Form of Indemnification Agreement entered into between the Registrant and each of its directors and executive officers | S-1/A | 333-186574 | 3/5/13 | 10.27 |
| 10.17 | Lease Agreement, dated as of November 16, 2006, by and between the Registrant and ARE-480 Arsenal Street, LLC, as amended on September 9, 2011, March 15, 2012, September 18, 2012, November 20, 2013, March 24, 2015 and June 18, 2015 | 10-Q | 001-35837 | 8/6/15 | 10.1 |
| 10.18 | Amendment, dated September 4, 2014, to Lease Agreement, dated as of November 16, 2006, by and between the Registrant and ARE-480 Arsenal Street, LLC, as amended | 10-Q | 001-35837 | 11/10/14 | 10.1 |
| 10.19 | Amendment, dated March 24, 2015, to Lease Agreement, dated as of November 16, 2006, by and between the Registrant and ARE-480 Arsenal Street, LLC, as amended | 10-Q | 001-35837 | 5/7/2015 | 10.1 |
| 10.20 | Amendment, dated June 18, 2015, to Lease Agreement, dated as of November 16, 2006, by and between the Registrant and ARE-480 Arsenal Street, LLC, as amended | 10-Q | 001-35837 | 8/6/2015 | 10.1 |
| 10.21† | License Agreement, dated as of August 3, 2006, by and between the Registrant and the President and Fellows of Harvard College, as amended | S-1 | 333-186574 | 2/11/13 | 10.20 |
| 10.22*† | Amendment, dated as of December 5, 2017, by and between the Registrant and the President and Fellows of Harvard College, as amended | | | | |
| 10.23† | Subcontract Agreement, dated as of February 1, 2012, by and between the Registrant and CUBRC, Inc. | S-1 | 333-186574 | 2/11/13 | 10.21 |
| 10.24† | Subcontract Agreement, dated as of September 30, 2011, by and between the Registrant and CUBRC, Inc. | S-1 | 333-186574 | 2/11/13 | 10.22 |
| 10.25# | Offer letter, dated as of June 20, 2015, by and between the Registrant and Christopher Watt | 10-K | 001-35837 | 2/25/16 | 10.17 |
| 10.26† | Master Manufacturing Services Agreement, dated June 14, 2017, by and between the Registrant and Patheon UK Limited | 10-Q | 001-35837 | 8/2/17 | 10.1 |
| 10.27† | Commercial Supply Agreement, dated October 16, 2017, by and between the Registrant and Finorga SAS | 10-Q | 001-35837 | 11/1/17 | 10.1 |
| 10.28*† | License Agreement, dated February 20, 2018, by and between the Registrant and Everest Medicines Limited | | | | |
| 10.29# | Offer letter, dated as of December 22, 2010, by and between the Registrant and Patrick T. Horn | S-1 | 333-186574 | 2/11/13 | 10.13 |
| 10.30# | Amendment to the Offer letter, dated March 5, 2014, by and between the Registrant and Patrick Horn | 10-Q | 001-35837 | 5/12/14 | 10.4 |

| Exhibit Number | Description | Incorporated by Reference from | | | |
|---|---|---|---|---|---|
| | | Registrant's Form | File No. | Date Filed with the SEC | Exhibit Number |
| 10.31#* | Offer letter, dated as of March 1, 2018, by and between the Registrant and Larry Edwards | | | | |
| 21.1* | Subsidiaries of the Registrant | | | | |
| 23.1* | Consent of Ernst & Young LLP | | | | |
| 31.1* | Chief Executive Officer—Certification pursuant to Rule 13a-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002 | | | | |
| 31.2* | Principal Financial Officer—Certification pursuant to Rule 13a-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002 | | | | |
| 32.1* | Chief Executive Officer—Certification pursuant to Rule 13a-14(a) of the Securities Exchange Act of 1934 and 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002 | | | | |
| 32.2* | Principal Financial Officer—Certification pursuant to Rule 13a-14(a) of the Securities Exchange Act of 1934 and 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002 | | | | |
| 101.INS* | XBRL Instance Document | | | | |
| 101.SCH* | XBRL Taxonomy Extension Schema Document | | | | |
| 101.CAL* | XBRL Taxonomy Extension Calculation Linkbase Document | | | | |
| 101.DEF* | XBRL Taxonomy Extension Definition Linkbase Document | | | | |
| 101.LAB* | XBRL Taxonomy Extension Label Linkbase Document | | | | |
| 101.PRE* | XBRL Taxonomy Extension Presentation Linkbase Document | | | | |

* Filed herewith.
\# Indicates management contract or compensatory plan or arrangement.
† Confidential treatment requested as to certain portions, which portions have been omitted and filed separately with the Securities and Exchange Commission.

**SIGNATURES**

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

TETRAPHASE PHARMACEUTICALS, INC.

Date: March 6, 2018

By: /s/ Guy Macdonald
Guy Macdonald
*President & Chief Executive Officer*
*(Principal Executive Officer)*

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

| Signature | Title | Date |
|---|---|---|
| /s/ Guy Macdonald<br>**Guy Macdonald** | Director, President and Chief Executive Officer<br>*(Principal Executive Officer)* | March 6, 2018 |
| /s/ Kamalam Unninayar<br>**Kamalam Unninayar** | Chief Financial Officer<br>*(Principal Financial and Accounting Officer)* | March 6, 2018 |
| /s/ L. Patrick Gage<br>**L. Patrick Gage, Ph.D.** | Chairman | March 6, 2018 |
| /s/ Garen Bohlin<br>**Garen Bohlin** | Director | March 6, 2018 |
| /s/ Jeffrey A. Chodakewitz<br>**Jeffrey A. Chodakewitz** | Director | March 6, 2018 |
| /s/ John G. Freund<br>**John G. Freund** | Director | March 6, 2018 |
| /s/ Geraldine Henwood<br>**Geraldine Henwood** | Director | March 6, 2018 |
| /s/ Nancy Wysenski<br>**Nancy Wysenski** | Director | March 6, 2018 |

TETRAPHASE PHARMACEUTICALS
Tetraphase Pharmaceuticals, Inc.
480 Arsenal Street, Suite 110
Watertown, MA 02472

**Exhibit 10.13**

December 21, 2017

Larry Tsai
[address]
[address]

Dear Larry:

On behalf of Tetraphase Pharmaceuticals, Inc. (the "Company"), I am very pleased to present you with this amended and restated offer letter in connection with our offer to promote you to the position of Chief Medical Officer. The purpose of this letter is to summarize the terms of your continued employment with the Company in this new appointment, should you accept our offer.

1. **Employment**. Effective December 29, 2017 (the "Effective Date"), you will be employed to serve on a full-time basis in the position of Chief Medical Officer, reporting directly to me as President and Chief Executive Officer, Tetraphase Pharmaceuticals, Inc. As Chief Medical Officer, you will have such duties and responsibilities as are customary for such position and such other duties and responsibilities as may be assigned to you by the Company. You agree to continue to devote your full business time, best efforts, skill, knowledge, attention, and energies to the advancement of the Company's business and interests and to the performance of your duties and responsibilities as an employee of the Company.

2. **Base Compensation**. As of the Effective Date, your base salary will be increased to the rate of $15,577 per bi-weekly pay period (equivalent to an annualized rate of $405,000), less all applicable federal, state, and local taxes and withholdings, such base salary to be paid in installments in accordance with the Company's standard payroll practices. Such base salary may be adjusted from time to time in accordance with normal business practices and in the sole discretion of the Company.

3. **Bonus**. If the Board of Directors approves an annual bonus for fiscal year 2018 or any fiscal year thereafter, you may be eligible for a discretionary retention and performance bonus award of up to 40% of your annualized base salary in such year (the "Target Bonus"). The bonus award, if any, will be based on both individual and corporate performance and will be determined by the Board of Directors of the Company in its sole discretion. In any event, in order to be eligible for and to earn a bonus, if any, you must be an active employee of the Company on the date such bonus is distributed, as it also serves as an incentive to remain employed by the Company. Any bonus that the Board determines to be payable for a fiscal year will be paid before March 15th of the next fiscal year.

4. **Benefits**. You will continue to participate in any and all benefit programs that the Company establishes and makes available to its employees from time to time, provided that you are eligible under (and subject to all provisions of) the plan documents governing those programs. Such benefits may include: participation in group medical and dental insurance programs, term life insurance, long-term disability insurance and participation in the Company's 401(k) plan. The

benefits made available by the Company, and the rules, terms, and conditions for participation in such benefit programs, may be changed by the Company at any time and from time to time without advance notice (other than as required by such programs or under law). With respect to vacation time, you will begin to accrue vacation at 1.67 days/month or the equivalent of a maximum of 4 weeks per calendar year. Vacation may be taken at such times as may be approved by the Company. Your accrual and use of vacation time will also be subject to any and all vacation policies and procedures that the Company establishes from time to time.

5. **Stock Incentive Program.** You will continue to be eligible to participate in the Company's stock incentive program. In connection with your acceptance of this promotion and subject to approval by the Company's Board of Directors, the Company will grant to you an option to purchase 150,000 shares of the Company's Common Stock (subject to adjustment for stock splits, combinations, or other recapitalizations) which will vest (i.e., become exercisable) 6.25% of the shares every three-months, subject to your continued employment by the Company. The option exercise price will be equal to the fair market value of one share of Common Stock on the date of grant of the option as determined by the Company's Board of Directors. In addition, if you accept this offer of promotion to Chief Medical Officer and also subject to approval of the Board of Directors, the Company will grant you 40,000 Performance Based Restricted Stock Units (PRSUs). The option grant and the PRSUs will be issued pursuant to the Company's 2013 Stock Incentive Plan, the stock option agreement covering the option and the Performance Based Restricted Stock Unit agreement covering the PRSUs.

6. **At-Will Employment**. This letter shall not be construed as an agreement, either express or implied, to continue to employ you for any stated term, and shall in no way alter the Company's policy of employment at will, under which both you and the Company remain free to terminate the employment relationship at any time, for any reason, with or without cause, and with or without notice. Although your job duties, title, compensation and benefits, as well as the Company's personnel policies and procedures, may change from time to time, the "at-will" nature of your employment may only be changed by a written agreement signed by you and the principal executive officer of the Company, which expressly states the intention to modify the at-will nature of your employment. Similarly, nothing in this letter shall be construed as an agreement, either express or implied, to pay you any compensation or grant you any benefit beyond the end of your employment with the Company, except to the extent explicitly set forth in Section 7 hereof.

7. **Severance Benefits.** Notwithstanding your status as an at-will employee, in the event that the Company (or, as may be applicable, an acquiring or succeeding company) terminates your employment without "Cause," or you terminate your employment with the Company (or, as may be applicable, an acquiring or succeeding company) for "Good Reason" (each term as defined in Exhibit A and in either case a "Qualifying Termination"), you will be eligible for the benefits outlined in either sub-section A or subsection B (the "Severance Benefits"), subject to the terms set forth in this letter agreement:

(A)If a Qualifying Termination occurs prior to or more than twelve months following a Change in Control Event (as defined in Exhibit A), the Company will provide to you as severance pay an amount equal to twelve (12) months of your then-current base salary (subject to all applicable federal, state and local taxes and withholdings and payable over a twelve -month

period in accordance with the Company's regular payroll practices). In addition, should you timely elect and be eligible to continue receiving group medical coverage pursuant to applicable "COBRA" law, and so long as the Company can provide such benefit without violating the nondiscrimination requirements of applicable law, the Company will, until the earlier of (x) the date that is twelve (12) months following your termination date and (y) the date you (or, as applicable, your beneficiaries) become eligible for coverage through a new employer, continue to pay the share of the premium for such coverage that is paid by the Company for active and similarly-situated employees who receive the same type of coverage (provided that the Company will not pay more each month than the monthly amount it was paying for your coverage when your employment ended). The remaining balance of any premium costs shall timely be paid by you on a monthly basis (or such other basis as is required by the Company) for as long as, and to the extent that, you remain eligible for COBRA continuation.

(B) If a Qualifying Termination occurs upon or during the twelve month period commencing upon a Change in Control Event, the Company will provide to you as severance pay an amount equal to the sum of (i) twelve (12) months of your then-current base salary (subject to all applicable federal, state and local taxes and withholdings and payable over a twelve -month period in accordance with the Company's regular payroll practices) and (ii) an amount equal to 100% of your then-current annual Target Bonus (subject to all applicable federal, state and local taxes and withholdings and payable in a lump sum). In addition, should you timely elect and be eligible to continue receiving group medical coverage pursuant to applicable "COBRA" law, and so long as the Company can provide such benefit without violating the nondiscrimination requirements of applicable law, the Company will, until the earlier of (x) the date that is twelve (12) months following your termination date and (y) the date you (or, as applicable, your beneficiaries) become eligible for coverage through a new employer, continue to pay the share of the premium for such coverage that is paid by the Company for active and similarly-situated employees who receive the same type of coverage (provided that the Company will not pay more each month than the monthly amount it was paying for your coverage when your employment ended). The remaining balance of any premium costs shall timely be paid by you on a monthly basis (or such other basis as is required by the Company) for as long as, and to the extent that, you remain eligible for COBRA continuation. Further, the vesting of all stock options held by you on the date of termination shall be accelerated, such that such stock options shall become 100% fully vested and exercisable.

Your receipt of severance pay and benefits as set forth in this Section 7 is conditioned upon your full compliance with the Non-Solicitation Agreement (as defined in Section 8 below), your timely execution of a separation and release of claims agreement prepared by and satisfactory to the Company (which will include, at a minimum, a release by you of all releasable claims, non-disparagement and cooperation obligations, and reaffirmation of your continuing obligations under the Non-Solicitation Agreement) (the "Release"), and any applicable revocation period with respect to the Release expiring without revocation within 60 days (or such shorter period as may be directed by the Company) following your termination date. If the Release has been executed and any applicable revocation period has expired prior to the 60th day following your termination, then the severance payments and benefits shall commence (or in the case of any lump sum payment, be paid) on the first regular pay date after any applicable revocation period has expired (but no earlier than the 30th day following your termination date); provided, however, that if the 60th day following your termination occurs in the calendar year following the

calendar year during which your termination occurs, then the severance payments shall commence (or in the case of any lump sum payment, be paid) no earlier than January 1 of such subsequent calendar year. The provision of severance pay and benefits hereunder shall be subject to the terms and conditions set forth in Section 11 hereto. In the event you breach your obligations under the Release or the Non-Solicitation Agreement, you will have no right to receive, and the Company shall not provide to you, any severance pay or benefits following the date of such breach. Such cessation of payments and benefits shall be in addition to, and not in lieu of, any and all other remedies, whether at law or in equity, available to the Company for such breach.

8. **Non-Solicitation, Non-Disclosure and Developments Agreement.** As a condition of your continued employment and promotion, you reaffirm your obligations under the Non-Solicitation, Non-Disclosure and Developments Agreement (the "Non-Solicitation Agreement") which you previously signed in connection with your employment, a copy of which is enclosed with this letter.

9. **Company Policies and Procedures**. As an employee of the Company, you remain required to comply with all Company policies and procedures. Violations of the Company's policies may lead to immediate termination of your employment. Further, the Company's premises, including all workspaces, furniture, documents, and other tangible materials, and all information technology resources of the Company (including computers, data and other electronic files, and all internet and email) remain subject to oversight and inspection by the Company at any time. Company employees should have no expectation of privacy with regard to any Company premises, materials, resources, or information.

10. **Other Agreements and Governing Law**. You represent that you are not bound by any employment contract, restrictive covenant or other restriction preventing you from continuing employment with or carrying out your responsibilities for the Company hereunder, or which is in any way inconsistent with the terms of this letter. Please note that this amended and restated offer letter is your formal offer of continued employment and supersedes any and all prior or contemporaneous agreements, discussions and understandings, whether written or oral, relating to the subject matter of this letter or your employment with the Company, including without limitation the previous offer letter between you and the Company dated March 14, 2014. The resolution of any disputes under this letter will be governed by Massachusetts law.

11. **Section 409A of the Code.**

Subject to the provisions in this Section 11, any severance payments or benefits under this letter will begin only upon the date of your "separation from service" (determined as set forth below) which occurs on or after the date of termination of your employment. The following rules shall apply with respect to distribution of the payments and benefits, if any, to be provided to you under this letter.

(a) It is intended that each installment of the severance payments and benefits provided under this letter shall be treated as a separate "payment" for purposes of Section 409A of the Internal Revenue Code and the guidance issued thereunder ("Section 409A"). Neither you nor the Company will have the right to accelerate or defer the delivery of any such payments or benefits except to the extent specifically permitted or required by Section 409A.

(b) The determination of whether and when your separation from service from the Company has occurred shall be made and in a manner consistent with and based on the presumptions set forth in, Treasury Regulation Section 1.409A-1(h). Solely for purposes of this paragraph, "Company" shall include all persons with whom the Company would be considered a single employer under Section 414(b) and 414(c) of the Internal Revenue Code.

(c) If, as of the date of your separation from service from the Company, you are not a "specified employee" (within the meaning of Section 409A), then each installment of the severance payments and benefits provided under this letter shall be made on the dates and terms set forth in this letter.

(d) If, as of the date of your separation from service from the Company, you are a "specified employee" (within the meaning of Section 409A), then:

(i) Each installment of the severance payments and benefits due under this letter that, in accordance with the dates and terms set forth herein, will in all circumstances, regardless of when your separation from service occurs, be paid within the short-term deferral period (as defined under Section 409A) shall be treated as a short-term deferral within the meaning of Treasury Regulation Section 1.409A-1(b)(4) to the maximum extent permissible under Section 409A and shall be paid on the dates and terms set forth in this letter; and

(ii) Each installment of the severance payments and benefits due under this letter that is not described in Section 11(d)(i) and that would, absent this subsection, be paid within the six-month period following your separation from service from the Company shall not be paid until the date that is six months and one day after such separation from service (or, if earlier, your death), with any such installments that are required to be delayed being accumulated during the six-month period and paid in a lump sum on the date that is six months and one day following your separation from service and any subsequent installments, if any, being paid in accordance with the dates and terms set forth herein; provided, however, that the preceding provisions of this sentence shall not apply to any installment of payments or benefits if and to the maximum extent that that such installment is deemed to be paid under a separation pay plan that does not provide for a deferral of compensation by reason of the application of Treasury Regulation 1.409A-1(b)(9)(iii) (relating to separation pay upon an involuntary separation from service). Any installments that qualify for the exception under Treasury Regulation Section 1.409A-1(b)(9)(iii) must be paid no later than the last day of your second taxable year following the taxable year in which the separation from service occurs.

(e) All reimbursements and in-kind benefits provided under this letter shall be made or provided in accordance with the requirements of Section 409A to the extent that such reimbursements or in-kind benefits are subject to Section 409A, including, where applicable, the requirements that (i) any reimbursement is for expenses incurred during your lifetime (or during a shorter period of time specified in your offer letter), (ii) the amount of expenses eligible for reimbursement during a calendar year may not affect the expenses eligible for reimbursement in any other calendar year, (iii) the reimbursement of an eligible expense will be made on or before the last day of the calendar year following the year in which the expense is incurred and (iv) the right to reimbursement is not subject to set off or liquidation or exchange for any other benefit.

(f) Notwithstanding anything herein to the contrary, the Company makes no representation or warranty and shall have no liability to you or to any other person if the payments and benefits

provided in this letter are determined to constitute deferred compensation subject to Section 409A but that do not satisfy an exemption from, or the conditions of, that section.

If you agree with the terms of your continued employment in connection with your appointment to the position of Chief Medical Officer, as set forth herein, please sign the enclosed duplicate of this letter in the space provided below and return it to me. This offer is effective through December 28, 2017. If you do not accept this offer by such date, it will be deemed revoked.

On behalf of Tetraphase Pharmaceuticals, Inc.

Guy Macdonald
President and Chief Executive Officer

The foregoing correctly sets forth the terms of my continued at-will employment by the Company. I am not relying on any representations pertaining to my employment other than those set forth above.

/s/ Larry Tsai Date: December 27, 2017
Larry Tsai

**EXHIBIT A**

Definitions

For the purposes of this amended and restated offer letter:

(1) **"Cause"** shall mean: (a) a good faith finding by the Board of Directors of the Company in its sole discretion that you have (i) failed or refused to substantially perform your assigned duties for the Company, or failed or refused to comply in any material respect with the Company's material policies or procedures, which failure or violation is not cured (provided that the Company deems that such failure or violation is curable) within 20 days following written notice from the Company to you specifying the duties not performed or the nature of the violation, (ii) engaged in dishonesty, gross negligence or misconduct, or (iii) breached any employment agreement, confidentiality agreement, non-solicitation agreement, or other agreement entered into between you and the Company; or (b) your conviction of, or the entry of a pleading of guilty or *nolo contendere* by you to, any crime involving dishonesty or moral turpitude or any felony.

(2) **"Change in Control Event"** shall mean

(a) the acquisition by an individual, entity or group (within the meaning of Section 13(d)(3) or 14(d)(2) of the Securities Exchange Act of 1934, as amended (the "Exchange Act")) (a "Person") of beneficial ownership of any capital stock of the Company if, after such acquisition, such Person beneficially owns (within the meaning of Rule 13d-3 promulgated under the Exchange Act) 50% or more of the combined voting power of the then-outstanding securities of the Company entitled to vote generally in the election of directors (the "Outstanding Company Voting Securities"); provided, however, that for purposes of this subsection (a), the following acquisitions shall not constitute a Change in Control Event: (i) any acquisition directly from the Company (excluding an acquisition pursuant to the exercise, conversion or exchange of any security exercisable for, convertible into or exchangeable for common stock or voting securities of the Company, unless the Person exercising, converting or exchanging such security acquired such security directly from the Company or an underwriter or agent of the Company), or (ii) any acquisition by any employee benefit plan (or related trust) sponsored or maintained by the Company or any corporation controlled by the Company; or

(b) the consummation of a merger, consolidation, reorganization, recapitalization or statutory share exchange involving the Company or a sale or other disposition of all or substantially all of the assets of the Company (a "Business Combination"), unless, immediately following such Business Combination all or substantially all of the individuals and entities who were the beneficial owners of the Outstanding Company Voting Securities immediately prior to such Business Combination beneficially own, directly or indirectly, more than 50% of the combined voting power of the then-outstanding securities entitled to vote generally in the election of directors, respectively, of the resulting or acquiring corporation in such Business Combination (which shall include, without limitation, a corporation which as a result of such transaction owns the Company or substantially all of the Company's assets either directly or through one or more subsidiaries) in substantially the same proportions as their ownership of the Outstanding Company Voting Securities immediately prior to such Business Combination:

provided that, where required to avoid additional taxation under Section 409A, the event that occurs must also be a "change in the ownership or effective control of a corporation, or a change in the

ownership of a substantial portion of the assets of a corporation" as defined in Treasury Regulation Section 1.409A-3(i)(5).

(3) **"Good Reason"** shall occur if a Cause event has not occurred or has not been cured, to the extent curable, and if (x) you provide written notice to the Company of the event or change you consider to constitute "Good Reason" within 30 calendar days following its occurrence, (y) you provide the Company with a period of at least 30 calendar days to cure the event or change, and (z) the "Good Reason" persists following the cure period, and you actually resign within 60 calendar days following the event or change. An event or change constituting "Good Reason" shall be limited to any of the following that occur without your prior written consent: (a) a material diminution of your duties, authority or responsibilities, provided, however, that the assignment of different duties to you by the Company involving a reasonably comparable level of responsibility shall not, by itself, constitute "Good Reason," and provided, further, that a change in your duties, authority or responsibilities solely as a result of the Company's acquisition by or merger with another entity, if you continue to have a comparatively senior role relative to the Company or its successor following such event, shall not, by itself, constitute "Good Reason"; (b) a material diminution in your base compensation, or (c) the relocation of the principal place at which you provide services to the Company by at least 50 miles and to a location such that your daily commuting distance is increased.

**Exhibit 10.22**

Confidential Materials omitted and filed separately with the
Securities and Exchange Commission. Double asterisks denote omissions.

**Fourth Amendment to License Agreement**

This Fourth Amendment to License Agreement (this "Fourth Amendment") is entered into as of this 5th day of December, 2017 (the "Fourth Amendment Effective Date"), by and between Tetraphase Pharmaceuticals, Inc., a Delaware corporation, with its principal place of business at 480 Arsenal Street, Suite 110, Watertown, MA 02472 ("Licensee") and President and Fellows of Harvard College, Richard A. and Susan F. Smith Campus Center, Suite 727, 1350 Massachusetts Avenue, Cambridge, MA 02138 ("Harvard").

WHEREAS, the parties entered into a License Agreement as of August 3, 2006 (as previously amended, the "License Agreement"), pursuant to which Harvard granted to Licensee an exclusive license under Harvard Patent Rights and Harvard's interest in Joint Patent Rights (as such terms are defined in the License Agreement);

WHEREAS, on January 31, 2007, the parties amended the License Agreement (the "First Amendment") to include a new patent application [**] under Harvard Patent Rights;

WHEREAS, on April 6, 2010, the parties amended the License Agreement (the "Second Amendment") to include the Additional Patent Application (as defined in the Second Amendment) under Harvard Patent Rights;

WHEREAS, the parties agreed in a letter dated June 2, 2010 to include [**] for all purposes of the License Agreement as Additional Patent Rights (as defined in the Second Amendment);

WHEREAS, on February 18, 2011, the parties amended the License Agreement (the "Third Amendment") to include [**] under Additional Patent Rights; and

WHEREAS, the parties wish to amend Licensee's payment obligations under the License Agreement to assist Licensee in its efforts to enter into one or more partnerships for the development and/or commercialization of products based on the Harvard Patent Rights;

NOW, THEREFORE, the parties hereto, intending to be legally bound, hereby agree as follows:

1. Capitalized terms used in this Fourth Amendment that are not defined herein shall have the meanings set forth in the License Agreement.

2. Section 1.3 of the License Agreement is replaced in its entirety with the following:

   **1.3. "Combination Product"** shall mean a pharmaceutical preparation that includes one or more Non-Covered Components in addition to one or more Covered Components. All references to Licensed Product or Royalty Product, as applicable, in this Agreement shall be deemed to include Combination Product.

3. Section 1.4 of the License Agreement is replaced in its entirety with the following:

**1.4. "Covered Component"** shall mean any compound (or part thereof) the production, making, use, sale or importation of which (a) falls within the scope of a Valid Claim or (b) would infringe any claim (other than any claim that has at any time been rejected by any patent examiner) made at any time in any patent or patent application within the Licensed Patent Rights as if such claim were as of such time a Valid Claim.

4. Section 1.13 of the License Agreement is hereby replaced in its entirety with the following:

**1.13. "Infringed Patent"** shall mean an issued and unexpired patent (a) that has not been abandoned, held invalid, revoked, held or rendered unenforceable or lost through interference and (b) the claims of which would be infringed by Licensee's practice of the Harvard Patent Rights and/or Joint Patent Rights in the making, using, offering for sale, selling or importation of Licensed Products or Royalty Products, as applicable.

5. Section 1.22 of the License Agreement is replaced in its entirety with the following:

**1.22. "Net Sales"** shall mean the gross amount billed or invoiced by or on behalf of Licensee, its Affiliates and Sublicensees (in each case, the "Invoicing Entity") on sales, leases or other transfers of Licensed Products or Royalty Products, as applicable, less the following to the extent applicable on such sales, leases or other transfers of Licensed Products or Royalty Products, as applicable, and not previously deducted from the gross invoice price: (a) customary trade, quantity, and cash discounts to the extent actually allowed and taken; (b) amounts actually repaid or credited by reason of rejection or return of any previously sold, leased or otherwise transferred Licensed Products or Royalty Products, as applicable, and uncollectible portions of billed or invoiced amounts with respect to any previously sold, leased or otherwise transferred Licensed Products or Royalty Products, as applicable; (c) rebates, chargebacks, retroactive price reductions, allowances and fees actually paid or credited to customers, wholesalers, distributors, third party payors, governmental agencies, administrators and contractees with respect to Licensed Products or Royalty Products, as applicable, sold, leased or otherwise transferred; (d) transportation, freight and insurance charges that are paid by or on behalf of the Invoicing Entity; and (e) to the extent separately stated on purchase orders, invoices, or other documents of sale, any sales, value added or similar taxes, custom duties or other similar governmental charges levied directly on the production, sale, transportation, delivery, or use of a Licensed Product or Royalty Product, as applicable, that are paid by or on behalf of the Invoicing Entity, but not including any tax levied with respect to income; provided that:

(i) in any transfers of Licensed Products or Royalty Products, as applicable, among an Invoicing Entity, Affiliates of such Invoicing Entity and Sublicensees, not for the purpose of resale by any such Affiliate or Sublicensee, Net Sales shall be equal to the fair market value of the Licensed Products or Royalty Products, as applicable, so transferred, assuming an arm's length transaction made in the ordinary course of business; and

(ii) in the event that an Invoicing Party receives non-monetary consideration for any Licensed Products or Royalty Products, as applicable, or in the case of transactions not at arm's length with a non-Affiliate of such Invoicing Entity that is not a Sublicensee, Net Sales shall be calculated based on the fair market value of such consideration or transaction, assuming an arm's length transaction made in the ordinary course of business.

Sales of Licensed Products or Royalty Products, as applicable, by an Invoicing Party to an Affiliate of such Invoicing Party or to a Sublicensee for resale by such Affiliate or Sublicensee shall not be deemed Net Sales and Net Sales shall be determined based on the gross amount invoiced or billed by such Affiliate or Sublicensee on resale to an independent third party purchaser.

In the event that a Licensed Product or Royalty Product, as applicable, is sold in any country in the form of a Combination Product, Net Sales of such Combination Product will be adjusted by multiplying actual Net Sales of such Combination Product (i.e., Net Sales as determined above without regard to this paragraph) in such country by the fraction A/(A+B), where A is the average invoice price in such country, of a Licensed Product or Royalty Product, as applicable, containing the same strength of Covered Component(s) that is included in such Combination Product sold without the Non-Covered Components, if sold separately in such country, and B is the average invoice price of the Non-Covered Component(s) that is included in such Combination Product in such country, if sold separately in such country. If, in a specific country, either the Covered Component(s) or the Non-Covered Component(s) is not sold separately, the relative value of the Covered Component(s) and the Non-Covered Component(s) in the Combination Product shall be negotiated in and agreed upon in good faith by the parties in order to determine the appropriate ratio for calculating Net Sales with respect to such Combination Product in such country.

6. Section 1.30 of the License Agreement is replaced in its entirety with the following:

**1.30. "Sublicense"** shall mean: (a) any right granted, license given, or agreement entered into by Licensee to or with any other person or entity (or by a Sublicensee to or with a further Sublicensee permitted by Section 4.2.2.4) under or with respect to or permitting any use of any of the Licensed Patent Rights, or otherwise permitting the development, manufacture, marketing, distribution, use and/or sale of Licensed Products or Royalty Products; (b) any option or other right granted by Licensee to any other person or entity (or by a Sublicensee to a further Sublicensee permitted by Section 4.2.2.4) to negotiate for or receive any of the rights described under clause (a); or (c) any standstill or similar obligation undertaken by Licensee toward any other person or entity (or by a Sublicensee toward a further Sublicensee permitted by Section 4.2.2.4) not to grant any of the rights described in clause (a) or (b) to any third party; in each case regardless of whether such grant of rights, license given or agreement entered into is referred to or is described as a sublicense. For clarity, "Sublicense" does not include any implied license that may be deemed to be granted as part of a sale of a Licensed Product.

7. A new Section 1.34 is hereby added to the License Agreement as follows:

**1.34. "Licensee Valid Claim"** shall mean: (a) a claim of an issued and unexpired patent owned by Licensee, excluding any Joint Patent Rights, that has not been (i) held permanently revoked, unenforceable, unpatentable or invalid by a decision of a court or governmental body of competent jurisdiction, unappealable or unappealed within the time allowed for appeal, (ii) rendered unenforceable through disclaimer or otherwise, (iii) abandoned, or (iv) lost through an interference proceeding; or (b) a pending claim of a pending patent application owned by Licensee (in a particular country), excluding any Joint Patent Rights, that (i) has been asserted and continues to be prosecuted in good faith, (ii) has not been abandoned or finally rejected without the possibility of appeal or refiling and (iii) has not remained un-issued for a period of five or more years from the date of issuance of the first substantive patent office action considering the patentability of such claim by the applicable patent office in such country.

8. A new Section 1.35 is hereby added to the License Agreement as follows:

**1.35. "Royalty Product"** shall mean any product that contains, as an active pharmaceutical ingredient, (a) eravacycline, TP-271 or TP-6076 or (b) any compound, other than eravacycline, TP-271 or TP-6076, the composition or synthesis of which would infringe any claim (other than any claim that has at any time been rejected by any patent examiner) made at any time in any patent or patent application within the Licensed Patent Rights as if such claim were as of such time a Valid Claim. For the avoidance of doubt, each Royalty Product shall also be deemed a Licensed Product for so long as (and only for so long as) the manufacture, use, offer for sale, sale or importation of such Royalty Product would infringe a Valid Claim.

9. A new Section 1.36 is hereby added to the License Agreement as follows:

**1.36. "First Commercial Sale"** shall mean the first sale for end use or consumption of a product in a country after the granting of all approvals from the relevant Regulatory Authority(ies) necessary to market and sell such product in such country.

10. Section 6.4.1 of the License Agreement is replaced in its entirety with the following:

**6.4.1. Royalties.**

**6.4.1.1.** As partial consideration for the license granted hereunder, Licensee shall pay Harvard an amount equal to the following percentages of any Net Sales of Licensed Products, and Royalty Products that are not Licensed Products, in the United States and its districts, territories and possessions (the "**US Territory**"), made by Licensee and/or its Affiliates or Sublicensees:

**(a)** [**] percent ([**]%) of Net Sales made on Licensed Products; and

**(b)** [**] percent ([**]%) of Net Sales made on Royalty Products that are not Licensed Products.

**6.4.1.2.** As partial consideration for the license granted hereunder, Licensee shall pay Harvard an amount equal to the following percentages of (y) Net Sales of Licensed Products in each country outside of the US Territory (the "**Ex-US Territory**") made by Licensee and/or its Affiliates (but not Sublicensees):

**(a)** [**] percent ([**]%) of that portion of calendar year annual Net Sales of Licensed Products up to [**] U.S. Dollars ($[**]);

**(b)** [**] percent ([**]%) of that portion of calendar year annual Net Sales of Licensed Products in excess of [**] U.S. Dollars ($[**]) up to [**] U.S. Dollars ($[**]);

**(c)** [**] percent ([**]%) of that portion of calendar year annual Net Sales of Licensed Products in excess of [**] U.S. Dollars ($[**]) up to [**] U.S. Dollars ($[**]); and

**(d)** [**] percent ([**]%) of that portion of calendar year annual Net Sales of Licensed Products in excess of [**] U.S. Dollars ($[**]).

**6.4.1.3.** As partial consideration for the license granted hereunder, Licensee shall pay Harvard an amount equal to the following percentages of (y) Net Sales of Royalty Products that are not Licensed Products in each country in the Ex-US Territory made by Licensee and/or its Affiliates (but not Sublicensees):

**(a)** [**] percent ([**]%) of that portion of calendar year annual Net Sales of Royalty Products that are not Licensed Products up to [**] U.S. Dollars ($[**]);

**(b)** [**] percent ([**]%) of that portion of calendar year annual Net Sales of Royalty Products that are not Licensed Products in excess of [**] U.S. Dollars ($[**]) up to [**] U.S. Dollars ($[**]);

**(c)** [**] percent ([**]%) of that portion of calendar year annual Net Sales of Royalty Products that are not Licensed Products in excess of [**] U.S. Dollars ($[**]) up to [**] U.S. Dollars ($[**]); and

**(d)** [**] percent ([**]%) of that portion of calendar year annual Net Sales of Royalty Products that are not Licensed Products in excess of [**] U.S. Dollars ($[**]).

**6.4.1.4.** With respect to each Royalty Product (other than Licensed Products) containing eravacycline, royalties will be payable under Sections 6.4.1.1(b) and 6.4.1.3, as applicable, until the date fifteen (15) years after the First Commercial Sale of the first Royalty Product in the first country, after which no royalties shall be due on Net Sales of Royalty Products containing eravacycline. With respect to each Royalty Product (other than Licensed Products) containing any compound other than eravacycline (and not containing eravacycline), royalties will be payable under Sections 6.4.1.1(b) and 6.4.1.3, as applicable, on a country-by-country basis until the fifth anniversary of the expiration of the last Licensee Valid Claim that covers the composition of the first Royalty Product containing such compound in such country, after which no royalties shall be due on Net Sales of such Royalty Product in such country. With respect to each Licensed Product,

including each Royalty Product that is also a Licensed Product, royalties will be payable under Sections 6.4.1.1(a) and 6.4.1.2 on a country-by-country basis for so long as the making, using or selling of such Licensed Product is covered by a Valid Claim in the country in which such Licensed Product is made, used or sold, after which no royalties shall be due on such Licensed Product (except, if such Licensed Product is also a Royalty Product, to the extent set forth in the first two sentences of this Section 6.4.1.4). For clarity, no milestones will be due under Section 6.3 with respect to any Royalty Product that is not a Licensed Product.

**6.4.1.5.** The parties acknowledge that the consideration terms and structure set forth in this Section 6.4.1 (a) were agreed upon for convenience purposes with the intent of compensating Harvard for the rights granted under this Agreement, including with respect to the Licensed Patent Rights and other valuable intellectual property licensed and/or transferred to Licensee, and the key role such rights and intellectual property will have in the activities of Licensee and its ability to enter into strategic relationships and (b) represent the fair market value of such rights as determined and agreed upon by the parties. For clarity, the terms of this Section 6.4.1 with respect to any Royalty Product shall survive the termination of this Agreement if such termination occurs prior to the end of the applicable royalty period for such Royalty Product.

11. Section 6.4.2 of the License Agreement is hereby deleted in its entirety.

12. Section 6.5 of the License Agreement is replaced in its entirety with the following:

**6.5. Sublicense Income.**

**6.5.1** As partial consideration for the license granted hereunder, Licensee shall pay Harvard (a) [**] percent ([**]%) of all Non-Royalty Sublicense Income, in connection with any Sublicense granted with rights to make and/or sell Licensed Products and/or Royalty Products solely in the Ex-US Territory, and (b) [**] percent ([**]%) of payments or other consideration that Licensee or any of its Affiliates receives in connection with a Sublicense that are royalties based on sales, leases or other transfers of Licensed Products or Royalty Products by or on behalf of Sublicensees in the Ex-US Territory ("**Ex-US Sublicensee Royalties**").

**6.5.2** As partial consideration for the license granted hereunder, Licensee shall pay Harvard an amount equal to the following percentages of Non-Royalty Sublicense Income received in connection with any Sublicense granted that includes rights to make and/or sell Licensed Products and/or Royalty Products in the US Territory, whether or not rights are granted in any ex-US Territory:

**(a)** if Licensee grants such Sublicense prior to the filing of an IND with respect to any Licensed Product or Royalty Product that is the subject of such Sublicense, Licensee shall pay Harvard an amount equal to [**] percent ([**]%) of all Non-Royalty Sublicense Income received in connection with such Sublicense;

**(b)** if Licensee grants such Sublicense after filing of an IND but prior to the Initiation of a Phase II Clinical Trial with respect to any Licensed Product or Royalty Product that is the subject of such Sublicense, Licensee shall pay Harvard an amount equal to [**] percent ([**]%) of all Non-Royalty Sublicense Income received in connection with such Sublicense; and

**(c)** if Licensee grants a Sublicense after the Initiation of a Phase II Clinical Trial with respect to any Licensed Product or Royalty Product that is the subject of such Sublicense, Licensee shall pay Harvard an amount equal to [**] percent ([**]%) of all Non-Royalty Sublicense Income received in connection with such Sublicense.

**6.5.3** Notwithstanding anything to the contrary in this Agreement, if Licensee or any of its Affiliates receives a payment constituting Non-Royalty Sublicense Income that is directly attributable to the occurrence of a milestone event described in Section 6.3 or a circumstance substantially equivalent to such milestone event and Licensee has paid or is obligated to pay to Harvard its due share of such Non-Royalty Sublicense Income under this Section 6.5, any amounts paid under Section 6.3 with respect to such milestone may be deducted from Non-Royalty Sublicense Income on which Licensee must pay fees to Harvard under this Section 6.5.

**6.5.4** Licensee's obligations under this Section 6.5 with respect to any Sublicense that includes rights to make and/or sell any Royalty Product shall expire on the expiration of Licensee's royalty payment obligations under Section 6.4.1 with respect to such Royalty Product. Licensee's obligations under this Section 6.5 with respect to any Sublicense that includes rights to make and/or sell any Licensed Product that is not a Royalty Product shall expire on expiration of Licensee's royalty payment obligations under Section 6.4.1 with respect to such Licensed Product.

13. Section 7.1 of the License Agreement is replaced in its entirety with the following:

**7.1. Reports and Payments.**

**7.1.1. Reports.** Within [**] days after the conclusion of each Calendar Quarter commencing with the first Calendar Quarter in which Net Sales are generated or Non-Royalty Sublicense Income or Ex-US Sublicensee Royalties received, Licensee shall deliver to Harvard a report containing the following information (in each instance, with a Licensed Product-by-Licensed Product or Royalty Product-by-Royalty Product, as applicable, breakdown):

**(a)** the number of units of Licensed Products or Royalty Products, as applicable, sold by Licensee and its Affiliates in the US Territory and Ex-US Territory, and by Sublicensees in the US Territory, for the applicable Calendar Quarter;

**(b)** the gross amount billed for Licensed Products or Royalty Products, as applicable, sold by Licensee and its Affiliates in the US Territory and Ex-US Territory, and by Sublicensees in the US Territory, during the applicable Calendar Quarter;

**(c)** a calculation of Net Sales by Licensee and its Affiliates in the US Territory and Ex-US Territory, and by Sublicensees in the US Territory, for the applicable Calendar Quarter, including an itemized listing of applicable deductions; and

**(d)** the total amount payable to Harvard in U.S. Dollars on Net Sales by Licensee and its Affiliates in the US Territory and Ex-US Territory, and by Sublicensees in the US Territory, for the applicable Calendar Quarter, together with the exchange rates used for conversion.

In addition, Licensee shall include in each such report a statement of all Non-Royalty Sublicense Income and Ex-US Sublicensee Royalties and the amounts payable to Harvard in respect thereto for the applicable Calendar Quarter. Each such report shall be certified on behalf of Licensee as true, correct and complete in all material respects by Licensee's Chief Financial Officer or an executive level officer with comparable authority. If no amounts are due to Harvard for any Calendar Quarter, the report shall so state.

**7.1.2. Payment for Net Sales.** Within [**] days after the end of each Calendar Quarter, Licensee shall pay Harvard all amounts due with respect to Net Sales, Non-Royalty Sublicense Income and Ex-US Sublicensee Royalties for the applicable Calendar Quarter.

14. Section 7.3 of the License Agreement is replaced in its entirety with the following:

**7.3. Records.** Licensee shall maintain, and shall cause its Affiliates and, with respect to the US Territory, Sublicensees to maintain, complete and accurate records of Licensed Products and Royalty Products that are made, used or sold under this Agreement, any amounts payable to Harvard in relation to such Licensed Products and Royalty Products and all Non-Royalty Sublicense Income and Ex-US Sublicensee Royalties received by Licensee and its Affiliates, which records shall contain sufficient information to permit Harvard to confirm the accuracy of any reports or notifications delivered to Harvard under Section 7.1. Licensee, its Affiliates and/or its Sublicensees, as applicable, shall retain such records relating to a given Calendar Quarter for at least [**] years after the conclusion of that Calendar Quarter, during which time Harvard shall have the right, at its expense, to cause an independent, certified public accountant to inspect such records during normal business hours for the sole purpose of verifying any reports and payments delivered under this Agreement. Such accountant shall enter into a confidentiality agreement reasonably satisfactory to Licensee and shall not disclose to Harvard any information other than information relating to the accuracy of reports and payments delivered under this Agreement. The parties shall reconcile any underpayment or overpayment within [**] days after the accountant delivers the results of the audit. In the event that any audit performed under this Section 7.3 reveals an underpayment in excess of five percent (5%) in any calendar year, the audited entity shall bear the full cost of such audit. Harvard may exercise its rights under this Section 7.3 [**] per audited entity and only with reasonable prior notice to the audited entity.

15. Section 11.1 of the License Agreement is replaced in its entirety with the following:

**11.1. Term.** The term of this Agreement shall commence on the Effective Date and, unless earlier terminated as provided in this Article 11, shall continue in full force and effect (a) on a Licensed Product-by-Licensed Product and country-by-country basis until expiration of the last to expire Valid Claim of the Harvard Patent Rights and Joint Patent Rights and (b) on a Royalty Product-by-Royalty Product and country-by-country basis until expiration of Licensee's royalty payment obligations with respect to such Royalty Product in such country under this Agreement; provided, however, that, once the making, using or selling of any Licensed Product or Royalty Product in any country is not covered by a Valid Claim within the Licensed Patent Rights or a Licensee Valid Claim, as the case may be, the license granted by Harvard to Licensee under Section 4.1 with respect to such Licensed Product or Royalty Product, as applicable, in such country will be perpetual, irrevocable, freely sublicensable and freely transferrable.

16. Section 11.4 of the License Agreement is replaced in its entirety with the following:

**11.4. Survival.** The parties' respective rights, obligations and duties under Articles 7 and 10 and under this Article 11, as well as any rights, obligations and duties which by their nature extend beyond the expiration or termination of this Agreement, shall survive any expiration or termination of this Agreement. In addition, Licensee's obligations under Section 6.5 with respect to any Sublicense granted prior to termination of the Agreement that includes rights to make and/or sell any Royalty Product shall survive termination of this Agreement and shall continue in full force and effect until the expiration of Licensee's royalty payment obligations under Section 6.4.1 with respect to such Royalty Product. Harvard's obligations under Section 12.15 shall survive expiration or termination of this Agreement. The terms of Section 6.4.1 shall survive termination of this Agreement.

17. All other terms and conditions of the License Agreement shall remain unchanged and in full force and effect.

**IN WITNESS WHEREOF**, the parties have caused this Fourth Amendment to be executed by their duly authorized representatives as of the date first written above.

| **President and Fellows of Harvard College** | | **Tetraphase Pharmaceuticals, Inc.** | |
|---|---|---|---|
| By: | /s/ Isaac T. Kohlberg | By: | /s/ Guy Macdonald |
| Name: | Isaac T. Kohlberg | Name: | Guy Macdonald |
| Title: | Sr. Associate Provost,<br>Chief Technology Development Officer,<br>Office of Technology Development<br>Harvard University | Title: | CEO |

**Exhibit 10.28**

Confidential Materials omitted and filed separately with the
Securities and Exchange Commission. Double asterisks denote omissions.

CONFIDENTIAL

**LICENSE AGREEMENT**

**BY AND BETWEEN**

**TETRAPHASE PHARMACEUTICALS, INC.**

**AND**

**EVEREST MEDICINES LIMITED**

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LIST OF EXHIBITS



LIST OF SCHEDULES

# LICENSE AGREEMENT

THIS **LICENSE AGREEMENT** (this "**Agreement**") is made and entered into as of February 20, 2018 ("**Effective Date**") between Tetraphase Pharmaceuticals, Inc., a corporation organized and existing under the laws of Delaware with a principal place of business at 480 Arsenal Street, Suite 110, Watertown, MA 02472 (" **Tetraphase**"), and Everest Medicines Limited, an exempted company organized and existing under the laws of Cayman Islands, with a principal place of business at Suite 4508, 45F, Tower 2, Plaza 66, 1266 Nanjing Xi Lu, Shanghai 200040, China ("**Licensee**").

Tetraphase and Licensee may be referred to herein individually as a "**Party**" and collectively as the "**Parties**".

## RECITALS

**WHEREAS**, Tetraphase is the owner of, or otherwise controls, the Tetraphase Technology in the Territory (each as defined below);

**WHEREAS**, Licensee has expertise in the development of biopharmaceutical products and has regulatory and commercial capabilities in the Territory, and is interested in obtaining an exclusive license to Develop and Commercialize the Licensed Products in the Territory, and a right to negotiate for the right to Manufacture the Licensed Products in the Territory (each as defined below); and

**WHEREAS**, the Parties desire to collaborate to Develop, Manufacture and Commercialize the Licensed Products in the Territory;

**NOW THEREFORE**, the Parties agree as follows:

## ARTICLE I.

## DEFINITIONS

**Section 1.01** "**Accounting Standards**" means, with respect to (a) Licensee or any of its Affiliates or sublicensees, U.S. GAAP, consistently applied, or (b) Tetraphase or any of its Affiliates or licensees, generally accepted accounting principles applicable to such entity, consistently applied.

**Section 1.02** **"Affiliate"** means, with respect to an entity, any corporation or other business entity controlled by, controlling, or under common control with such entity, with "control" meaning (direct) or indirect beneficial ownership of at least fifty percent (50%) of the voting stock of, or at least a fifty percent (50%) interest in the income of, the applicable entity (or such lesser percentage that is the maximum allowed to be owned by a foreign entity in a particular jurisdiction and is sufficient to grant the holder of such voting stock or interest the power to direct the management and policies of such entity) or (b) possession, directly or indirectly, of the power to direct the management and policies of an entity, whether through ownership of voting securities, by contract relating to voting rights or corporate governance or otherwise.

**Section 1.03** **"API"** means active pharmaceutical ingredient.

**Section 1.04** **"API Bulk Drug Substance"** means the Licensed Compound in bulk form manufactured for use as an API.

**Section 1.05** **"Business Day"** means a day other than (a) a Saturday or a Sunday or (b) a day on which banking institutions in Boston, Massachusetts, or in Beijing, China are authorized or required by Law to remain closed.

**Section 1.06** "**CFDA**" means the China Food and Drug Administration, including its divisions and the Center for Drug Evaluation, and local counterparts thereto, and any successor agency or authority thereto having substantially the same function.

**Section 1.07** **"cIAI"** means complicated intra-abdominal infection.

**Section 1.08** **"Commercialization" or "Commercialize"** means, with respect to a pharmaceutical product, any and all activities directed to the marketing, promotion, importation, distribution, pricing, Reimbursement Approval, offering for sale, or sale of such pharmaceutical product, and interacting with Regulatory Authorities regarding the foregoing. Commercialization shall exclude Research and Manufacturing.

**Section 1.09** **"Commercialization Plan"** means the annual plan for Commercialization of Licensed Products in the Field in the Territory and the activities to be conducted by Licensee relating thereto, including detailed plans for sales and marketing after launch, sales and marketing budgets and sales forecasts and target numbers regarding reach and frequency of sales performance, which plan Licensee shall ensure is at all times consistent with the terms and conditions of this Agreement and all In-License Agreements.

**Section 1.10** **"Commercially Reasonable Efforts"** means, with respect to the Development, Manufacture or Commercialization of any Licensed Product, those efforts and resources, including reasonably necessary personnel, equivalent to the efforts that a similarly situated biopharmaceutical company would typically devote to a product owned by it of similar market potential, profit potential and strategic value and at a comparable stage in development or product life to such Licensed Product, as applicable, based on conditions then prevailing and taking into account issues of safety and efficacy, product profile, difficulty in developing such Licensed Product, as applicable, competitiveness of alternative Third Party products in the marketplace, the patent or other proprietary position of such Licensed Product, as applicable, the regulatory structure involved and the potential profitability of such Licensed Product, as applicable, but not taking into account any payment obligations under this Agreement.

**Section 1.11** **"Competing Product"** means any product that is in the tetracycline class and intended to treat any indication that is, at the relevant time, in the Field, but excluding (a) the Licensed Compound, (b) the Licensed Product, and (c) TP-6076.

**Section 1.12** **"Confidential Information"** means, subject to **Section 12.02(a)-(d)**, Know-How and any technical, scientific, trade, research, manufacturing, business, financial, marketing, product, supplier, intellectual property or other information that may be disclosed by one Party or any of its Affiliates to the other Party or any of its Affiliates, regardless of whether

such information is specifically designated as confidential and regardless of whether such information is in written, oral, electronic, or other form. Notwithstanding the foregoing, subject to **Section 12.02(a)-(d)**, all information that (a) was disclosed prior to the Effective Date by or on behalf of either Party or any of its Affiliates under, and subject to, the Confidentiality Agreement by and between Tetraphase and Licensee, dated August 18, 2017 ("**Confidentiality Agreement**"), (b) is "Proprietary Information" as defined in the Confidentiality Agreement, and (c) is not subject to Section 5(a), 5(b), 5(c) or 5(d) of the Confidentiality Agreement as of the Effective Date (as defined in this Agreement), shall be deemed "Confidential Information" hereunder.

**Section 1.13** **"Controlled"** means, subject to **Section 16.02 (Acquisitions)**, with respect to a Party or any of its Affiliates, and any Know-How, Patent Right, Regulatory Documents or other intellectual property right, that such Party or Affiliate, as the case may be, has the ability (other than pursuant to a license granted to such Party or Affiliate, as the case may be, under this Agreement) to grant to the other Party a license or sublicense to, or other right with respect to, such Know-How, Patent Right, Regulatory Documents or other intellectual property right without violating the terms of any pre-existing agreement or other pre-existing arrangement with any Third Party; *provided, however*, that, if a Party or any of its Affiliates obtains rights to any Know-How, Patent Rights, Regulatory Documents or other intellectual property rights through any license agreement that is not an In-License Agreement, such Party or Affiliate shall only be deemed to "Control" such Know-How, Patent Rights or other intellectual property rights, as applicable, for purposes of this Agreement, (a) to the extent such license agreement does not conflict with any provision of this Agreement and (b) to the extent such license agreement conflicts with this Agreement or includes additional obligations not set forth in this Agreement, the other Party agrees in writing to be bound by all applicable obligations set forth in such license agreement (including the obligation to pay royalties, milestones, sublicense income and the *pro rata* share of the other costs associated with such license agreement to the extent that such costs apply to any activity by or on behalf of such other Party (or any of its Affiliates or (sub)licensees) under this Agreement).

**Section 1.14** **"Cost of Goods Sold"** or **"COGS"** means, with respect to a particular Licensed Product, the Manufacturing cost for such Licensed Product, which (a) to the extent such Licensed Product is Manufactured by Tetraphase or its Affiliates, shall approximate a reasonable definition of cost of goods sold for such Licensed Product with no markup and shall be further specified in the Supply Agreement and (b) to the extent such Licensed Product is Manufactured by a Third Party, the actual, documented out-of-pocket costs paid to such Third Party for the Manufacture of such Licensed Product.

**Section 1.15** **"Cover"**, **"Covering"** or **"Covered"** means, with respect to a product, composition, technology, process or method and a Patent Right, that, in the absence of ownership of, or a license granted under, a claim in such Patent Right, the manufacture, use, offer for sale, sale or importation of such product or composition or the practice of such technology, process or method would infringe such claim (or, in the case of a claim of a pending patent application, would infringe such claim if it were to issue as a claim of an issued patent).

**Section 1.16** [Intentionally Left Blank].

**Section 1.17** **"Development"** means all (a) clinical development and regulatory activities regarding a pharmaceutical compound or product, as the case may be, including (i) clinical trials of such pharmaceutical compound or product; (ii) preparation, submission, review, and development of data or information for the purpose of submission to a Regulatory Authority to obtain authorization to conduct clinical trials or obtain Regulatory Approval of such pharmaceutical product; and (iii) Medical Affairs with respect to such pharmaceutical compound or product, and (b) with respect to the activities of Licensee, solely (i) to the extent agreed upon within the JSC or required by a relevant Regulatory Authority in the Territory to obtain or maintain a Regulatory Approval contemplated by this Agreement, and (ii) on a non-exclusive basis unless otherwise agreed by the Parties, non-clinical or pre-clinical activities conducted in support of the foregoing, the Development Plan, the Launch Plan or the Commercialization Plan. Development shall include clinical trials initiated following receipt of Regulatory Approval, but shall exclude Research (except as set forth in clause (b)), Manufacturing and Commercialization.

**Section 1.18** **"Development Plan"** means the plan setting out activities to be undertaken in Developing the Licensed Products in the Field in the Territory, together with timelines for such activities, including the proposed clinical trials and regulatory plans, as well as outlining the key elements involved in obtaining Regulatory Approval of the Licensed Products in the Field in the Territory, as may be amended from time to time in accordance with **Section 4.01 (Development in the Field in the Territory)**, which plan (a) Licensee shall ensure is at all times consistent with the terms and conditions of this Agreement and all In-License Agreements, (b) Licensee shall ensure is focused on efficiently obtaining Regulatory Approval for Licensed Products in each Jurisdiction in the Territory, while taking into consideration potential impacts on the Development or Commercialization of any Eravacycline Product outside of the Territory or Field and (c) shall include in reasonable detail (i) all Development activities reasonably anticipated to be undertaken by the Licensee Entities, (ii) the endpoints for all clinical trials contemplated by such plan, (iii) which clinical trial is intended to be a pivotal trial and (iv) all regulatory activities and interactions anticipated to be conducted by the Licensee Entities in support of Regulatory Approval of the Licensed Products in the Field in the Territory, including all planned Regulatory Filings to be submitted in connection with such approvals.

**Section 1.19** **"Dollars" or "$"** means the legal tender of the U.S.

**Section 1.20** **"Drug Approval Application"** means a New Drug Application as defined in the FD&C Act, or an equivalent application filed with any Regulatory Authority in any country other than the United States.

**Section 1.21** **"Eravacycline Materials"** means API Bulk Drug Substance, intermediates required to Manufacture Finished Drug Product, and Finished Drug Product.

**Section 1.22** **"Eravacycline Product"** means any pharmaceutical product that has the Licensed Compound as at least one API.

**Section 1.23** **"Existing Regulatory Documents"** means Regulatory Documents Controlled by Tetraphase or any of its Affiliates as of the Effective Date.

**Section 1.24** **"FDA"** means the U.S. Food and Drug Administration or any successor agency thereto.

**Section 1.25** **"FD&C Act"** means the U.S. Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 301 et seq., as amended from time to time.

**Section 1.26** **"Field"** means (a) the treatment of (i) cIAI and (ii) any indication other than cIAI for which any Tetraphase Entity files a Drug Approval Application for any Licensed Product in the United States or anywhere else outside the Territory and (b) any other human indication agreed by the Parties pursuant to **Section 2.08 (Field or Licensed Product Expansion)**.

**Section 1.27** **"Finished Drug Product"** means the finished product formulation of a Licensed Product, containing API Bulk Drug Substance, filled into unit packages for final labeling and packaging, and as finally labeled and packaged in a form ready for administration.

**Section 1.28** **"First Commercial Sale"** means, for each Licensed Product in the Field in a Jurisdiction, the first sale for end use or consumption of such Licensed Product in the Field in such Jurisdiction by any Licensee Entity (or, following termination, solely for purposes of the "Royalty Term" definition set forth in **Section 2.01(c)**, any Tetraphase Entity) after the granting of Regulatory Approval for such Licensed Product in the Field in such Jurisdiction by the relevant Regulatory Authorities. Sales prior to receipt of Regulatory Approval for such Licensed Product, such as so-called "treatment IND sales," "named patient sales," and "compassionate use sales," shall not be construed as a First Commercial Sale.

**Section 1.29** **"Generic Product"** means, with respect to a given Licensed Product in a Jurisdiction, any pharmaceutical preparation that (a) contains Licensed Compound as its sole active pharmaceutical ingredient, (b) is marketed for sale in such Jurisdiction by a Third Party (other than a Licensee Entity) that is not authorized directly or indirectly by any Licensee Entity, and (c) receives Regulatory Approval for sale in such Jurisdiction in reliance, based in whole or in part, on the prior Regulatory Approval (or on safety or efficacy data submitted in support of such prior Regulatory Approval) of such Licensed Product as determined by the applicable Regulatory Authority or is approved for sale in reliance, in whole or in part, on the existing drug standard already approved by the applicable Regulatory Authority (unless a Licensee Entity authorizes the applicable Third Party to access, use or reference, such Regulatory Approval, data or drug standard).

**Section 1.30** **"Good Clinical Practices" or "GCP"** means the then-current good clinical practice standards, practices, and procedures promulgated or endorsed by any applicable Regulatory Authority as set forth in the guidelines imposed by such Regulatory Authority, as may be updated from time to time.

**Section 1.31** **"Good Laboratory Practices" or "GLP"** means the then-current good laboratory practice standards, practices, and procedures promulgated or endorsed by any applicable Regulatory Authority as set forth in the guidelines imposed by such Regulatory Authority, as may be updated from time to time.

**Section 1.32** **"Governmental Authority"** means any federal, national, multinational, state, provincial, country, city or local government or any court, arbitrational tribunal, administrative agency or commission or government authority acting under the authority of any federal, national, multinational, state, provincial, country, city or local government.

**Section 1.33** **"Harvard Agreement"** means the License Agreement by and between Tetraphase and the President and Fellows of Harvard College ("**Harvard**"), dated as of August 3, 2006, as amended from time to time.

**Section 1.34** **"In-License Agreement"** means (a) the Harvard Agreement or (b) any other agreement between Tetraphase or any of its Affiliates, on the one hand, and one or more Third Parties, on the other hand, pursuant to which Tetraphase or any of its Affiliates acquires Control of any Know-How or Patent Rights that are Tetraphase Know-How or Tetraphase Patent Rights that the Parties mutually agree in writing is an In-License Agreement.

**Section 1.35** **"IND"** means an Investigational New Drug application for submission to the FDA or any equivalent counterpart application in any country other than the United States, including all supplements and amendments thereto.

**Section 1.36** **"Invention"** means any invention, process, method, composition of matter, article of manufacture, discovery or finding that is conceived or reduced to practice (whether or not patentable).

**Section 1.37** **"Joint Invention"** means any Invention that is jointly conceived or reduced to practice during the Term by any employee, agent or contractor of Tetraphase or any of its Affiliates, on the one hand, and any employee, agent or contractor of Licensee or any of its Affiliates, on the other hand.

**Section 1.38** **"Joint Know-How"** means any Know-How that is identified, conceived, reduced to practice, discovered, authored or developed jointly by any employee, agent or contractor of Tetraphase or any of its Affiliates, on the one hand, and any employee, agent or contractor of Licensee or any of its Affiliates, on the other hand

**Section 1.39** **"Joint Patent Rights"** means all Patent Rights claiming Joint Inventions or Covering Joint Know-How.

**Section 1.40** **"Joint Technology"** means Joint Know-How and Joint Patent Rights.

**Section 1.41** **"Jurisdiction"** means each of the following: mainland China, Taiwan, Hong Kong, Macau, South Korea or Singapore.

**Section 1.42** **"Know-How"** means Inventions, discoveries, trade secrets, information, experience, data, formulas, procedures, technology and results (whether or not patentable), including discoveries, formulae, practices, methods, knowledge, know-how, processes, experience and test data (including physical, chemical, biological, toxicological, pharmacological, clinical and veterinary data), dosage regimens, control assays, product specifications, analytical and quality control data, and marketing, pricing, distribution cost and sales data or descriptions; but excluding Patent Rights.

**Section 1.43** **"Launch Plan"** means the strategic plan for the Licensed Products in the Field in the Territory that details the activities to be conducted prior to launch, plans for launch, and activities to be conducted after launch.

**Section 1.44** **"Law"** means any law, statute, rule, regulation, order, judgment, standard or ordinance of any Governmental Authority.

**Section 1.45** **"Licensed Compound"** means the compound identified on **Schedule 1.45**, and any metabolite, salt, ester, hydrate, solvate, isomer, enantiomer, free acid form, free base form, crystalline form, co-crystalline form, amorphous form, pro-drug (including ester pro-drug) form, racemate, polymorph, chelate, stereoisomer, tautomer or optically active form of any of the foregoing.

**Section 1.46** **"Licensed Product"** means any pharmaceutical product that (a) has the Licensed Compound as its sole API and (b) is in a form (i) for which any Tetraphase Entity (A) is Developing in the United States as of the Effective Date or (B) files a Drug Approval Application in the United States or anywhere else outside the Territory after the Effective Date, or (ii) agreed by the Parties pursuant to **Section 2.08 (Field or Licensed Product Expansion)**.

**Section 1.47** **"Licensee Entity"** means, as applicable, (a) Licensee, (b) any of Licensee's Affiliates or (c) any direct or indirect sublicensee or subcontractor of Licensee or any of Licensee's Affiliates with respect to any Licensed Product.

**Section 1.48** **"Licensee In-License Agreement"** means any agreement pursuant to which any Licensee Entity has in-licensed or otherwise acquired the right to practice, or in-licenses or otherwise acquires the right to practice, any Know-How related to, or Patent Rights that Cover, any of the Licensed Products in the Field in the Territory or that would result in royalties or other amounts that would be payable to a Third Party based on the Development, Manufacture or Commercialization of Licensed Products in the Field in the Territory.

**Section 1.49** **"Licensee Know-How"** means all Know-How that is both (a) Controlled as of the Effective Date or during the Term by Licensee or any of its Affiliates and (b) necessary or reasonably useful for the Research, Development, Manufacture or Commercialization of the Licensed Compound or any Eravacycline Product; but excluding all Joint Inventions and Joint Know-How. For the avoidance of doubt, Licensee Know-How shall include (x) any Know-How developed during clinical trials conducted by a Licensee Entity in the Field in the Territory, (y) all Licensee Product Data and (z) all Licensee Regulatory Documents.

**Section 1.50** **"Licensee Patent Rights"** means all Patent Rights that both (a) are Controlled as of the Effective Date or during the Term by Licensee or any of its Affiliates, and (b) Cover the Licensed Compound or any Eravacycline Product or their respective Research, Development, Manufacture or Commercialization (or are necessary or reasonably useful for such Research, Development, Manufacture or Commercialization); but excluding all Joint Patent Rights.

**Section 1.51** **"Licensee Regulatory Documents"** means Regulatory Documents Controlled by Licensee or any of its Affiliates at any time during the Term that (a) relate to the Licensed Compound or a Licensed Product in the Territory and (b) are necessary or reasonably useful for a Tetraphase Entity to prepare a Regulatory Filing with respect to any Eravacycline Product outside of the Territory. For the avoidance of doubt, upon any expiration or termination of this Agreement (in its entirety or in one or more Jurisdictions), any Regulatory Documents that, at the time of such expiration or termination, constitute Licensee Regulatory Documents in the applicable Jurisdiction(s) shall remain Licensee Regulatory Documents after such expiration or termination.

**Section 1.52** **"Licensee Technology"** means Licensee Know-How and Licensee Patent Rights.

**Section 1.53** **"Manufacture"** or **"Manufacturing"** means, as applicable, all activities associated with the production, manufacture, process of formulating, processing, filling, finishing, packaging, labeling, shipping, importing or storage of pharmaceutical compounds or materials, including process development, process validation, stability testing, manufacturing scale-up, pre-clinical, clinical and commercial manufacture and analytical development, product characterization, quality assurance and quality control development, testing and release.

**Section 1.54** **"Medical Affairs"** means communications with key opinion leaders, medical education, symposia and other medical programs and communications.

**Section 1.55** **"Net Sales"** means the gross invoice price of a particular Licensed Product sold or otherwise transferred to a Third Party by any Licensee Entity for consideration, reduced by the following amounts to the extent such items are customary under industry practices and to the extent such amounts are, with respect to any deduction described in clause (a), (b), (d), (f) or (g), included in the gross invoiced sales price or documented in the invoices or otherwise properly documented by the relevant Licensee Entity, or, with respect to any deduction described in clause (c) or (e), documented in the invoices issued to the relevant Third Party or paid to the relevant Third Party following the initial date of invoicing and properly documented by the relevant Licensee Entity with such Third Party, in each case in accordance with Accounting Standards:

(a) normal and customary trade, quantity and prompt settlement discounts (including chargebacks and allowances) actually allowed and taken directly with respect to such unit of Licensed Product;

(b) tariffs, duties, excises, value added tax and other sales taxes imposed by any Governmental Authority upon and paid by the applicable Licensee Entity with respect to the sale, transportation, delivery, use, exportation, or importation of such Licensed Product (which does not include income, withholding or similar taxes);

(c) amounts repaid or credited by reason of rejection, return or recall of goods, or rebates;

(d) freight, postage, shipping and insurance expenses to the extent that such items are included in the gross amount invoiced;

(e) the portion of administrative fees paid during the relevant time period to group purchasing organizations or pharmaceutical benefit managers relating to such Licensed Product;

(f) any invoiced amounts that are not collected by such Party, its Affiliates or its or their sublicensees, including bad debts and uncollectable invoiced amounts actually written off in accordance with applicable Accounting Standards, *provided* that (i) any such amounts subsequently collected will be included in Net Sales and (ii) the amounts deducted under this subsection (f) shall not exceed [**] percent ([**]%) of gross sales of the relevant Licensed Product in the relevant calendar quarter; and

(g) any other similar and customary deductions that are consistent with applicable Accounting Standards; *provided* that the following provisions will also apply to the calculation of Net Sales hereunder:

(A) Any of the deductions listed above that involves a payment by the particular Licensee Entity will be taken as a deduction in the calendar quarter in which the payment is accrued by such entity. For purposes of determining Net Sales, a Licensed Product will be deemed to be sold when invoiced and a "sale" will not include transfers or dispositions of such Licensed Product for pre-clinical or clinical purposes or compassionate use, and shall not include transfers or dispositions of a commercially reasonable quantity of samples of such Licensed Product, in each case, without charge. A Licensee Entity's transfer of any Licensed Product to an Affiliate of Licensee or to a sublicensee will not result in any Net Sales unless (i) the transferee is an end user or (ii) subject to the immediately preceding sentence, the next transfer to a Third Party that is not a sublicensee is included in Net Sales.

(B) In the case of pharmacy incentive programs, hospital performance incentive programs, chargebacks, disease management programs, similar programs or any discounts, in each case that are credited, discounted or reimbursed on a portfolio of product offerings, all such rebates, discounts and other forms of reimbursements will be allocated among all the products in such portfolio on the basis on which such rebates, discounts and other forms of reimbursements were actually granted or, if such basis cannot be determined, in accordance with the applicable Licensee Entity's existing allocation method, in each case consistently applied across all such Licensee Entity's products; *provided* that any such allocation will be done in accordance with applicable Law, including any price reporting Laws.

(C) Subject to the above, Net Sales will be calculated in accordance with the standard internal policies and procedures of Licensee, its Affiliates or its or their sublicensees; *provided* that such policies and procedures (1) are in accordance with applicable Accounting Standards and (2) do not favor other products being Developed, Manufactured or Commercialized by or on behalf of Licensee or its Affiliates or its or their sublicensees that are not Licensed Products.

**Section 1.56** **"Patent Rights"** means (a) all patents and patent applications (including provisional applications) in any country or jurisdiction, and (b) any substitutions, divisions, continuations, continuations-in-part, reissues, renewals, registrations, confirmations, re-examinations, extensions, supplementary protection certificates and the like.

**Section 1.57** **"Phase 1 Clinical Trial"** means a clinical trial in humans which provides for the first introduction into humans of a pharmaceutical product, to generate information on product safety, tolerability, pharmacological activity or pharmacokinetics, as described in Federal Regulation 21 C.F.R. §312.21(a) and its foreign equivalents.

**Section 1.58** **"Phase 2 Clinical Trial"** means a clinical trial in humans of the safety, dose ranging and efficacy of a pharmaceutical product, as described in Federal Regulation 21 C.F.R. §312.21(b) and its foreign equivalents.

**Section 1.59** **"Phase 3 Clinical Trial"** means a controlled clinical trial, or a portion of a controlled clinical trial, in humans of the efficacy and safety of a pharmaceutical product, which study (in its entirety or portion, as applicable) is prospectively designed to demonstrate statistically whether such product is effective and safe for use in a manner sufficient to file a Drug Approval Application, as described in Federal Regulation 21 C.F.R. §312.21(c) and its foreign equivalents. For the sake of clarity, with respect to what is commonly called a phase 2/3 trial, the Phase 3 Clinical Trial definition is met upon the first patient, first visit in the portion of such study that is prospectively designed to demonstrate statistically whether such pharmaceutical product is effective and safe for use in a manner sufficient to file an Drug Approval Application, as described in Federal Regulation 21 C.F.R. §312.21(c) and its foreign equivalents.

**Section 1.60** **"Product Trademark"** means any Trademark for use in connection with the Commercialization of any Licensed Product. "Product Trademark" specifically excludes the corporate names and logos of the Parties and their Affiliates. "Product Trademark" includes each Tetraphase Trademark and each Licensee Trademark, as applicable.

**Section 1.61** **"Regulatory Approval"** means, with respect to a particular regulatory jurisdiction, any approval, product or establishment license, registration or authorization of any Governmental Authority necessary for the commercial sale of a pharmaceutical product in such regulatory jurisdiction.

**Section 1.62** **"Regulatory Authority"** means, in a particular country or jurisdiction, any applicable Governmental Authority involved in granting Regulatory Approval in such country or jurisdiction, including (a) in the United States, the FDA and any other applicable Governmental Authority in the United States having jurisdiction over pharmaceutical products, (b) in Europe, the European Medicines Agency ("**EMA**"), (c) in mainland China, the CFDA and (d) any other applicable Governmental Authority in the Territory having jurisdiction over pharmaceutical products.

**Section 1.63** **"Regulatory Documents"** means all (a) applications (including all INDs, clinical trial applications and drug approval applications), registrations, licenses, authorizations and approvals (including Regulatory Approvals); (b) correspondence and reports submitted to or received from Regulatory Authorities (including minutes and official contact reports relating to any communications with any Regulatory Authority) and all supporting documents with respect thereto, including all regulatory drug lists, advertising and promotion documents, adverse event files and complaint files; and (c) preclinical, clinical and other data results, analyses, publications, and reports contained or referred to in any of the foregoing; in each case ((a), (b) and (c)) relating to the Licensed Compound or a Licensed Product. For the avoidance of doubt, Regulatory Documents include Regulatory Approvals and Regulatory Filings.

**Section 1.64** **"Regulatory Filings"** means all applications, filings, dossiers and the like submitted to a Regulatory Authority for the purpose of Developing, Manufacturing or Commercializing a product, including obtaining Regulatory Approval from that Regulatory Authority. Regulatory Filings include all INDs, Drug Approval Applications and other Regulatory Approval applications.

**Section 1.65** **"Reimbursement Approval"** means an approval, agreement, determination, or other decision by any applicable Regulatory Authority or other Governmental Authority that establishes prices at which a pharmaceutical product may be priced, or will be reimbursed by the Regulatory Authorities or other applicable Governmental Authorities, in a particular country or jurisdiction.

**Section 1.66** **"Research"** means all activities relating to discovery, evaluation or preclinical research (including identification of potential candidates, synthesis and testing by *in vitro* or *in vivo* assays).

**Section 1.67** **"Safety Data Exchange Agreement"** means that agreement between the Parties regarding receipt, investigation and reporting of product complaints, adverse events, product recalls, and any other information related to the safety of the Licensed Products as set forth in **Section 10.03** (**Adverse Drug Events**).

**Section 1.68** "**Tax**" means any present or future taxes, levies, imposts, duties, tariffs, charges, assessments or fees of any nature imposed by a Governmental Authority in the exercise of its taxing power (including interest, penalties and additions thereto), including value-added tax ("**VAT**") and withholding tax.

**Section 1.69** **"Territory"** means any Jurisdiction; but excluding any Jurisdiction that is, at the relevant time, in the Terminated Territory.

**Section 1.70** **"Tetraphase Entity"** means, as applicable, (a) Tetraphase, (b) any of Tetraphase's Affiliates or (c) any direct or indirect licensee, sublicensee or contractor of Tetraphase or any of Tetraphase's Affiliates with respect to the Licensed Compound or any Licensed Product (other than any Licensee Entity).

**Section 1.71** **"Tetraphase Know-How"** means all Know-How that is both (a) Controlled as of the Effective Date or during the Term by Tetraphase or any of its Affiliates and (b) necessary or reasonably useful for the Development or Commercialization of any Licensed Product in the Field in the Territory; but excluding all Joint Inventions and Joint Know-How. For the avoidance of doubt, Tetraphase Know-How shall include (x) any Know-How developed during clinical trials relating to Licensed Product conducted by any Tetraphase Entity, to the extent such Know-How is Controlled by Tetraphase or any of its Affiliates, (y) all Tetraphase Product Data and (z) all Tetraphase Regulatory Documents.

**Section 1.72** **"Tetraphase Patent Rights"** means all Patent Rights that both (a) are Controlled as of the Effective Date or during the Term by Tetraphase or any of its Affiliates in the Territory, and (b) Cover any Licensed Product, or its Development or Commercialization (or are necessary or reasonably useful for its Development or Commercialization), in the Field in the Territory; but excluding all Joint Patent Rights. Tetraphase Patent Rights as of the Effective Date include those listed in Exhibit A.

**Section 1.73** **"Tetraphase Regulatory Documents"** means Regulatory Documents Controlled by Tetraphase or any of its Affiliates as of the Effective Date or at any time during the Term that (a) relate to the Licensed Compound or a Licensed Product and (b) are **necessary** or reasonably useful for a Licensee Entity to prepare a Regulatory Filing with respect to the Licensed Product in the Field in the Territory; but excluding any Regulatory Filings submitted to a Regulatory Authority for the purpose of Manufacturing any product.

**Section 1.74** **"Tetraphase Technology"** means Tetraphase Know-How and Tetraphase Patent Rights.

**Section 1.75** **"Third Party"** means any person or entity other than the Parties and their Affiliates.

**Section 1.76** **"Total Indirect Costs"** means Third Party costs and expenses incurred to conduct multi-region clinical trials that are not directly allocable to a Party's territory, such as fees for data management that are not specific to a territory or clinical site.

**Section 1.77** **"TP-6076"** means, as applicable, (a) (i) the compound identified on **Schedule 1.77**, or (ii) any metabolite, salt, ester, hydrate, solvate, isomer, enantiomer, free acid form, free base form, crystalline form, co-crystalline form, amorphous form, pro-drug (including ester pro-drug) form, racemate, polymorph, chelate, stereoisomer, tautomer or optically active form of any of the foregoing, or (b) any pharmaceutical product containing TP-6076, alone or with other APIs.

**Section 1.78** **"Trademark"** means any trademark, trade name, service mark, service name, brand, domain name, trade dress, logo, slogan or other indicia of origin or ownership, including the goodwill and activities associated with each of the foregoing.

**Section 1.79** **"U.S."** or **"United States"** means the United States of America.

**Section 1.80** **"Valid Claim"** means (a) any claim of any Patent Right that has issued, is unexpired and has not been rejected, revoked or held unenforceable or invalid by a final, non-appealable (or unappealed within the time allowable for appeal) decision of a court or other Governmental Authority of competent jurisdiction or (b) any claim of any patent application that has (i) been pending for five (5) years or less from the date of issuance of the first substantive patent office action considering the patentability of such claim by the applicable patent office in the applicable country and (ii) not been cancelled, withdrawn, abandoned or finally rejected by an administrative agency action from which no appeal can be taken; *provided* that if after the earliest possible date for requesting examination in such country the patentee fails to request examination by such patent office within sixty (60) days after the licensed Party requests the patentee to do so, such five (5) year period shall run from the date of the licensed Party's request that the patentee request examination.

| Additional Defined Terms | Section |
|---|---|
| | |
| Arbitration Request | Section 15.01(a) |
| Agreement | Preamble |
| Alliance Manager | Section 3.12 |
| Acquired Party | Section 16.02 |
| Acquirer | Section 16.02 |
| Acquiring Party | Section 2.06(b) |
| Acquisition | Section 16.02 |
| Bankrupt Party | Section 14.05(a) |
| Breaching Party | Section 14.03 |
| Breach Notice | Section 14.03 |
| CMC | Section 2.04(b) |
| Committee | Section 3.01(a) |
| Confidentiality Agreement | Section 1.12 |
| Effective Date | Preamble |
| EMA | Section 1.62 |
| Event of Bankruptcy | Section 14.05(a) |
| Exclusive Negotiation Period | Section 2.09 |
| Executive Officer | Section 3.08 |
| Existing Patents | Section 11.03(a) |
| FCPA | Section 11.06(b)(i) |
| Government Official | Section 11.06(a)(A) |
| Harvard | Section 1.33 |
| Harvard Indemnitees | Section 13.05 |
| Harvard Patent Rights | Section 9.04(a)(i) |

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|---|---|
| ICC | Section 15.01(c) |
| ICH | Section 10.02 |
| In-License Agreement | Section 11.03(c) |
| Indemnified Party | Section 13.03 |
| Indemnifying Party | Section 13.03 |
| Infringement Activity | Section 9.05(a) |
| JCC | Section 3.01(a) |

| Additional Defined Terms | Section |
|---|---|
| | |
| JDC | Section 3.01(a) |
| JSC | Section 3.01(a) |
| Licensee | Preamble |
| Licensee Indemnitees | Section 13.01 |
| Licensee Product Data | Section 2.04(b) |
| Licensee Trademarks | Section 6.06(b) |
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| Non-Breaching Party | Section 14.03 |
| Other Covered Party | Section 11.06(a)(B) |
| Other Party | Section 14.05(a) |
| Party or Parties | Preamble |
| PRC | Section 9.09 |
| Recipient | Section 12.02 |
| Representatives | Section 12.01 |
| Royalty Term | Section 8.04(b) |
| Rules | Section 15.01 |
| Severed Clause | Section 16.05 |
| Subcommittee | Section 3.01(b) |
| Supply Agreements | Section 7.02 |
| Term | Section 14.01 |
| Terminated Territory | Section 14.07(b) |
| Tetraphase | Preamble |
| Tetraphase Indemnitees | Section 13.02 |
| Tetraphase Product Data | Section 2.04(b) |
| Tetraphase Trademarks | Section 6.06(a) |
| TP-6076 Data Package | Section 2.09 |
| TP-6076 Negotiation Notice | Section 2.09 |
| VAT | Section 1.68 |

**Section 1.81** **Interpretation**. (a) Whenever any provision of this Agreement uses the word "including," "include," "includes," or "*e.g.*," such word shall be deemed to mean "including without limitation" and "including but not limited to"; (b)

"herein," "hereby," "hereunder," "hereof" and other equivalent words shall refer to this Agreement in its entirety and not solely to the particular portion of this Agreement in which any such word is used; (c) a capitalized term not defined herein but reflecting a different part of speech from that of a capitalized term which is defined herein shall be interpreted in a correlative manner; (d) wherever used herein, any pronoun or pronouns shall be deemed to include both the singular and plural and to cover all genders; (e) the recitals set forth at the start of this Agreement, along with the schedules and the exhibits to this Agreement, and the terms and conditions incorporated in such recitals and schedules and exhibits, shall be deemed integral parts of this Agreement and all references in this Agreement to this Agreement shall encompass such recitals and schedules and exhibits and the terms and conditions incorporated in such recitals and schedules and exhibits; *provided* that, in the event of any conflict between the terms and conditions of this Agreement and any terms and conditions set forth in the recitals, schedules or

exhibits, the terms of this Agreement shall control; (f) in the event of any conflict between the terms and conditions of this Agreement and any terms and conditions that may be set forth on any order, invoice, verbal agreement or otherwise, the terms and conditions of this Agreement shall govern; (g) this Agreement shall be construed as if both Parties drafted it jointly, and shall not be construed against either Party as principal drafter; (h) unless otherwise provided, all references to Sections, Articles and Schedules in this Agreement are to Sections, Articles and Schedules of and to this Agreement; (i) any reference to any Law shall mean such Law as in effect as of the relevant time, including all rules and regulations thereunder and any successor Law in effect as of the relevant time, and including the then-current amendments thereto; (j) wherever used, the word "shall" and the word "will" are each understood to be imperative or mandatory in nature and are interchangeable with one another; (k) references to a particular person or entity include such person's or entity's successors and assigns to the extent not prohibited by this Agreement; (l) references to Tetraphase's knowledge shall be taken to refer to the knowledge of Tetraphase's senior management team as of the Effective Date having made no particular inquiry; (m) except where the context otherwise requires, the word "or" is used in the inclusive sense that is typically associated with the phrase "and/or"; (n) the captions and table of contents used herein are inserted for convenience of reference only and shall not be construed to create obligations, benefits or limitations; (o) the word "year" means any consecutive twelve (12) month period, unless otherwise specified; (p) reference to an "indication" means, with respect to a product, any use to which such product is intended to be put for the treatment, prevention, mitigation, cure or diagnosis of a recognized disease or condition, or of a manifestation of a recognized disease or condition, or for the relief of symptoms associated with a recognized disease or condition, in each case for any size patient population, which, if approved in the U.S., would be reflected in the "Indications and Usage" section of labeling pursuant to 21 C.F.R. §201.57(c)(2) or, to the extent applicable, any comparable labeling section outside the U.S., including any such use that is the subject to a clinical trial; (q) references to the "Field" mean any or all of the applicable indications described in the definition of "Field", in any size patient population; and (r) references to cAIA mean the treatment of cAIA in any size patient population.

## ARTICLE II.

## LICENSES; EXCLUSIVITY

**Section 2.01** **Grants of Licenses**.

(a) Subject to the terms and conditions of this Agreement (including **Section 4.05(z)**), Tetraphase hereby grants to Licensee an exclusive (including with regard to Tetraphase and its Affiliates), royalty-bearing, non-sublicensable (except in accordance with **Section 2.02 (Rights to Sublicense or Subcontract)**), non-transferrable (except in accordance with **Section 16.01 (Assignment)**) license under the Tetraphase Technology and Tetraphase's interest in t Jdint Technology to Develop and Commercialize Licensed Products in the Field in the Territory.

(b) Subject to the terms and conditions of this Agreement, to the extent permitted by applicable Law, Tetraphase hereby grants to Licensee an exclusive (including with regard to Tetraphase and its Affiliates), non-sublicensable (except in accordance with **Section 2.02 (Rights to Sublicense or Subcontract)**), non-transferrable (except in accordance with **Section 16.01 (Assignment)**) right of reference under the Tetraphase Regulatory Documents to Develop and Commercialize Licensed Products in the Field in the Territory.

(c) Subject to the terms and conditions of this Agreement, Licensee hereby grants to Tetraphase, (i) an exclusive (including with regard to Licensee and its Affiliates), royalty-free (subject to clause (ii)), fully-paid (subject to clause (ii)), freely transferrable, freely sublicensable, perpetual, irrevocable license under Licensee Technology and Licensee's interest in Joint Technology to Research, Develop, Manufacture and Commercialize the Licensed Compound, Eravacycline Materials and Eravacycline Products outside the Territory, and (ii) from and after any early termination of this Agreement (in one or more Jurisdictions or in its entirety), an exclusive (including with regard to Licensee and its Affiliates), freely transferrable, freely sublicensable, perpetual, irrevocable license under Licensee Technology and Licensee's interest in Joint Technology to Research, Develop, Manufacture and Commercialize the Licensed Compound, Eravacycline Materials and Eravacycline Products (other than any Licensed Product and Jurisdiction with respect to which Licensee retains a perpetual license pursuant to **Section 8.04(b)**) in the Terminated Territory; *provided* that (A) if this Agreement is terminated by Licensee pursuant to **Section 14.03 (Termination for Breach)**, Tetraphase shall pay Licensee a royalty of [**] percent ([**]%) of Net Sales of Licensed Products in the Terminated Territory, *mutatis mutandis*, with the provisions of **Section 8.04(b)** (second sentence only), **Section 8.04(c)**, **Section 8.04(d)**, **Section 8.05 (Royalty Payments and Reports)**, **Section 8.07 (Accounting)**, **Section 8.08 (Currency Conversion)**, **Section 8.09 (Methods of Payment)**, **Section 8.10 (Taxes)** and **Section 8.11 (Late Payments)** applying with respect thereto, *mutatis mutandis*; *provided* that (solely for the purposes of such royalty payment, *mutatis mutandis*, with such provisions) **"Royalty Term"** shall mean that period commencing on the effective date of termination and ending on the later of (i) expiration of the last-to-expire Valid Claim that is a composition of matter claim (for clarity, including a formulation claim) in the Licensee Patent Rights or Joint Patent Rights that Covers such Licensed Product in the Field in such Jurisdiction in the Terminated Territory, (ii) expiration of marketing or regulatory exclusivity with respect to such Licensed Product in such Jurisdiction in the Terminated Territory, (iii) ten (10) years from the date of First Commercial Sale of the applicable Licensed

Product in the Field in the applicable Jurisdiction in the Terminated Territory or (iv) five (5) years from the effective date of termination and (B) Tetraphase may, upon written notice to Licensee, terminate its license under this **Section 2.01(c)(ii)** and, thereby, terminate such royalty obligation.

(d) Subject to the terms and conditions of this Agreement (including **Section 2.01(a)**, **Section 2.01(b)**, **Section 2.01(c)**, **Section 2.01(e)**, **Section 2.01(f)**, **Section 2.06 (Exclusivity)** and **Section 8.04 (Royalties)**), and to the extent not already granted herein, each Party hereby grants, and shall cause its Affiliates to grant, to the other Party a worldwide, non-exclusive, royalty-free, fully-paid, freely sublicensable, freely transferrable right and license to exploit the Joint Technology in any manner without compensating or accounting to the other Party or its Affiliates.

(e) Subject to the terms and conditions of this Agreement, to the extent permitted by applicable Law, Licensee hereby grants to Tetraphase an exclusive (including with regard to Licensee and its Affiliates), non-sublicensable (except in accordance with **Section 2.02 (Rights to Sublicense or Subcontract)**), non-transferrable (except in accordance with **Section 16.01 (Assignment)**) right of reference under the Licensee Regulatory Documents to Develop and Commercialize Licensed Products outside the Territory.

(f) During the Term, Tetraphase shall not, and shall not grant to any of its Affiliates or any Third Party a license under the Tetraphase Technology and Tetraphase's interest in t Jdint Technology to, Develop or Commercialize any Eravacycline Product for any human use in the Territory.

**Section 2.02** **Rights to Sublicense or Subcontract**. Except as set forth in **Section 2.01(d)**, Licensee may not sublicense any of the rights granted to Licensee by Tetraphase hereunder, or subcontract any of Licensee's obligations hereunder, except with (a) Tetraphase's prior written consent, which consent may not be unreasonably withheld, delayed or conditioned (*provided* that Tetraphase's prior written consent shall not be required with respect to any such sublicense to an Affiliate of Licensee), and (b) to the extent required under the Harvard Agreement, Harvard's prior written consent. Whether or not Licensee is required to obtain Tetraphase's consent to sublicense any rights hereunder, Licensee shall remain responsible for the acts or omissions of any of its Affiliates or sublicensees with respect to this Agreement.

**Section 2.03** **No Other Rights and Retained Rights**. Nothing in this Agreement shall be interpreted to grant either Party any rights under any Patent Rights or Know-How owned by or licensed to the other Party that are not expressly granted herein, whether by implication, estoppel or otherwise. Any rights not expressly granted to a Party by the other Party under this Agreement are hereby retained by such other Party.

**Section 2.04** **Knowledge Transfer**.

(a) Within a reasonable time following the Effective Date (but, with respect to the Know-How identified in **Schedule 2.04**, no later than [**] days following the Effective Date, and, with respect to all other applicable Know-How, [**] days following the Effective Date), (i) Tetraphase shall provide to Licensee information describing the Development program for the Licensed Compound and Licensed Products, including all non-clinical and clinical data and other Know-How that are identified in **Schedule 2.04** or, in Tetraphase's reasonable determination, are necessary or reasonably useful for the Development or Commercialization of the Licensed Products in the Field in the Territory and (ii) Tetraphase shall use commercially reasonable efforts to make its qualified personnel reasonably available to Licensee, by telephone or other remote conferencing system or at Tetraphase's place of business and upon reasonable prior notice, for the purpose of discussing such information under this **Section 2.04** (**Knowledge Transfer**). Licensee shall reimburse Tetraphase for any reasonable out-of-pocket costs incurred by Tetraphase in fulfilling its obligations pursuant to clause (ii) of the immediately preceding sentence, and shall pay Tetraphase, at the rates set forth in Exhibit D, for each hour that any of Tetraphase's personnel spend answering questions or providing instruction pursuant to clause (ii) of the immediately preceding sentence, in each case within [**] days after the receipt of an invoice therefor; *provided* that the first [**] FTE hours of such support, in aggregate, shall be at no expense to Licensee.

(b) Subject to **Section 4.05(z)**, throughout the Term, Tetraphase shall make available to Licensee copies of Tetraphase Know-How, including research data and reports, regulatory materials and correspondence (including INDs and Drug Approval Applications), clinical and preclinical data, and chemistry, manufacturing and controls ("**CMC**") data, (collectively, the "**Tetraphase Product Data**") to the extent such Tetraphase Product Data is necessary or reasonably useful for any Licensee Entity to Develop or Commercialize any Licensed Product in the Field in the Territory. Throughout the Term, Licensee shall make available to Tetraphase copies of Licensee Know-How, including research data and reports, regulatory materials and correspondence (including INDs and Drug Approval Applications), clinical and preclinical data, and CMC data, (collectively, the "**Licensee Product Data**") to the extent such Licensee Product Data is necessary or reasonably useful for any Tetraphase Entity to Develop or Commercialize the Licensed Compound or any Eravacycline Product outside of the Territory or to Research or Manufacture the Licensed Compound or any Eravacycline Product.

(c) (i) Subject to **Section 4.05(z)**, Licensee shall be entitled at no cost to access, use, and reference the Tetraphase Regulatory Documents and Tetraphase Product Data for the Development and Commercialization of the Licensed Products in the Field in the Territory in accordance with this Agreement. (ii) The Tetraphase Entities shall be entitled at no cost to access, use and reference the Licensee Regulatory Documents and Licensee Product Data for the Development or Commercialization of the Licensed Compound and Eravacycline Products outside of the Territory and for the Research or Manufacture of the Licensed Compound and Eravacycline Products.

**Section 2.05** **In-License Agreements**. Licensee acknowledges and agrees that certain of the rights, licenses and sublicenses granted by Tetraphase to Licensee in this Agreement (including any sublicense rights) are subject to the terms of the In-License Agreements and the rights granted to the Third Party counterparties thereunder, the scope of the licenses granted to Tetraphase or any applicable Affiliate thereunder and the rights retained by such Third Party counterparties and any other Third Parties (including Governmental Authorities) set forth therein. Licensee shall, and shall ensure that each Licensee Entity shall, perform and take such actions to allow Tetraphase and its Affiliates to comply with their obligations under each In-License Agreement, only to the extent applicable to Licensee's rights or obligations under this Agreement, including Article 10 and Sections 4.2.3, 5.1 (first sentence only and solely with respect to the Development and Commercialization of Licensed Products in the Field in the Territory), 5.3, 6.3, 6.5, 7.1.1, 7.3, 9.1, and 12.2 of the Harvard Agreement as in effect on the Effective Date. Without limiting the foregoing, each Licensee Entity shall prepare and deliver to Tetraphase, or assist Tetraphase in preparing, any additional reports required under any In-License Agreement, in each case reasonably sufficiently in advance to enable Tetraphase and its Affiliates to comply with their obligations thereunder. Each Licensee Entity shall comply with each In-License Agreement. To the extent there is a conflict between the terms of any In-License Agreement and any rights granted to Licensee hereunder, the terms of the applicable In-License Agreement(s) shall control. Any breach by any Licensee Entity of any provision of any In-License Agreement applicable to any of them pursuant to this **Section 2.05 (In-License Agreements)** shall be deemed a material breach of this Agreement. To the extent permitted under the relevant In-License Agreement, Tetraphase shall provide Licensee with a copy of (a) any In-License Agreement executed after the Effective Date, promptly after Tetraphase identifies that such In-License Agreement is relevant to Licensee's rights and obligations under this Agreement, and (b) any amendment to any In-License Agreement previously provided to Licensee, promptly after such amendment is executed.

**Section 2.06** **Exclusivity**.

(a) General Covenants.

(i) During the Term and for [**] years after termination of this Agreement by Licensee pursuant to **Section 14.03 (Termination for Breach)** or **Section 14.05 (Termination for Bankruptcy and Rights in Bankruptcy)**, neither Tetraphase nor any of its Affiliates shall, itself or with or through any Third Party, without the prior written consent of Licensee, engage in any Development or Commercialization of any Competing Product in the Territory. For the avoidance of doubt, and without limiting the foregoing, during the Term, neither Tetraphase nor any of its Affiliates shall, itself or with or through any Third Party, without the prior written consent of Licensee, engage in any Development or Commercialization of the Licensed Compound or of any Eravacycline Product in the Territory (including advertising or promotional activities directed primarily to customers or other buyers or users located in the Territory or accepting orders from or selling in the Territory).

(ii) During the Term and for [**] years after termination of this Agreement by Tetraphase pursuant to **Section 14.02 (Termination for Patent Right Challenge)**, **Section 14.03 (Termination for Breach)** or **Section 14.05 (Termination for Bankruptcy and Rights in Bankruptcy)**, or for [**] after any other termination of this Agreement, neither Licensee nor any of its Affiliates shall, itself or with or through any Third Party, without the prior written consent of Tetraphase, engage in any Research, Development, Manufacture or Commercialization of any Competing Product in any country of the world, except with respect to the Development or Commercialization of any Licensed Product in the Field in the Territory in accordance with this Agreement. For the avoidance of doubt, and without limiting the foregoing, during the Term and for [**] years after termination of this Agreement, neither Licensee nor any of its Affiliates shall, itself or with or through any Third Party, without the prior written consent of Tetraphase, engage in any Development or Commercialization of the Licensed Compound or of any Licensed Product outside of the Field or outside of the Territory (including advertising or promotional activities directed primarily to customers or other buyers or users outside of the Field or located outside of the Territory or accepting orders from or selling outside of the Territory) or in any Research or Manufacture of the Licensed Compound or of any Eravacycline Product.

(b) If, during the term of the exclusivity covenant in **Section 2.06(a)**, a Party or any of its Affiliates acquires or is acquired by a Third Party (whether such acquisition occurs by way of a purchase of assets, merger, consolidation, change of control or otherwise) (such Party, the "**Acquiring Party**" for purposes of this **Section 2.06**) that is, at the time of such acquisition, Researching, Developing, Manufacturing or Commercializing a Competing Product in a manner that, if performed by the Acquiring Party or any of its Affiliates, would violate **Section 2.06(a)**, then the Acquiring Party or its applicable Affiliate will, no later than [**] days following the date of consummation of the relevant acquisition, notify the other Party in writing that the Acquiring Party or such Affiliate will:

(i) divest, whether by license or otherwise, its interest in the Competing Product to a Third Party, to the extent necessary to be in compliance with **Section 2.06(a)**, with no rights in such Competing Product retained by the Acquiring Party or any of its Affiliates; or

(ii) terminate the Research, Development, Manufacture and Commercialization of the Competing Product, to the extent necessary to be in compliance with **Section 2.06(a)**.

(c) If the Acquiring Party or any of its Affiliates notifies the other Party in writing that it or its relevant Affiliate intends to divest such Competing Product or terminate the Research, Development, Manufacture and Commercialization of the Competing Product as provided in **Section 2.06(b)**, then the acquiring Party or its relevant Affiliate will effect the consummation of such divestiture within [**] months or effect such termination within [**] months after the consummation of the relevant acquisition, subject to compliance with applicable Law, and will confirm to the other Party in writing when such divestiture or termination has been completed. The acquiring Party will keep the other Party reasonably informed of its and its Affiliates' efforts and progress in effecting such divestiture or termination until it is completed. Until such divestiture or termination occurs, the Acquiring Party shall keep its and its Affiliates' activities with respect to such Competing Product separate from their activities with respect to the Licensed Products.

(d) Each Licensee Entity will use commercially reasonable efforts to monitor and prevent exports of Licensed Products from the Territory for Development or Commercialization outside of the Territory using methods commonly used in the industry for such purpose, and shall promptly inform Tetraphase of any such exports from the Territory, and the actions taken to prevent such exports. Licensee shall take, and shall ensure that each Licensee Entity takes, reasonable actions requested in writing by Tetraphase that are consistent with Law to prevent such exports. If Licensee or any of its Affiliates or, to Licensee's or any of its Affiliates' knowledge, any other Licensee Entity receives a request or order to (i) Research or Manufacture any Licensed Compound or Eravacycline Product or (ii) Develop or Commercialize any Licensed Compound or Eravacycline Product outside of the Territory, Licensee shall immediately notify Tetraphase thereof, shall not accept such request or order, and shall direct the relevant individual or entity to Tetraphase. Tetraphase and its Affiliates will use commercially reasonable efforts to monitor and prevent exports of Licensed Products, from countries outside the Territory in which any of Tetraphase or its Affiliates, at the relevant time, directly and actively Developing or Commercializing any Eravacycline Product, for Development or Commercialization in the Territory, using methods commonly used in the industry for such purpose, and shall promptly inform Licensee of any such exports from any such country outside the Territory, and the actions taken to prevent such exports. If Tetraphase or, to Tetraphase's knowledge, any Tetraphase Entity receives a request or order to Develop or Commercialize any Licensed Product in the Field in the Territory, Tetraphase shall immediately notify Licensee thereof, shall not accept such request or order, and shall direct the relevant individual or entity to Licensee.

(e) Each Party agrees that the duration and scope of the covenants set forth in this **Section 2.06 (Exclusivity)** are reasonable. In the event that the arbitrator or any court determines that the duration or scope of any such provision is unreasonable and that any such provision is to that extent unenforceable, the Parties agree that such provision shall remain in full force and effect for the greatest time period and to the greatest scope that would not render it unenforceable. The Parties intend that the provisions of this **Section 2.06 (Exclusivity)** shall be deemed to be a series of separate covenants, one for each and every product, indication and jurisdiction where such provision is intended to be effective.

**Section 2.07** **Diligence.** Licensee shall use Commercially Reasonable Efforts to Develop and Commercialize Licensed Products in the Field in the Territory in accordance with this Agreement (including **Section 4.01 (Development in the Field in the Territory)** and **Section 6.04 (Commercialization Efforts)**).

**Section 2.08** **Field or Licensed Product Expansion.** Upon the written request of either Party, the Parties shall promptly discuss in good faith whether to expand the Field to include one or more additional indications in humans or to expand the definition of Licensed Product to include one or more additional formulations; *provided* that any such expansion pursuant to this **Section 2.08 (Field or Licensed Product Expansion)** shall be by mutual written agreement; *provided, further*, that the Parties hereby agree that such expansion of the Field or the definition of Licensed Product shall require no additional payment by Licensee; *provided*, for clarity, that (a) consistent with the definition of Net Sales set forth herein, any Net Sales of any additional Licensed Product or made for use in any indication added to the Field shall be included in the Net Sales used to calculate the achievement of the commercial milestones set forth in **Section 8.03 (Sales Milestone Payments)** and royalty payments owed pursuant to

**Section 8.04 (Royalties)** and (b) solely for purposes of any milestone events set forth in **Section 8.02 (Development Milestone Payment)** that have not been achieved as of the date on which the definition of "Field" is expanded pursuant to this **Section 2.08 (Field or Licensed Product Expansion),** all uses of the word "Field" in **Section 8.02 (Development Milestone Payment)** shall include all of the additional indications included in the expanded definition of "Field."

**Section 2.09** **ROFN.** Within [**] days after Tetraphase receives the final clinical study report for its first multiple ascending dose Phase 1 Clinical Trial of TP-6076, Tetraphase shall provide to Licensee (a) a true and complete copy of such clinical study report, (b) all material pre-clinical data with respect to TP-6076 in Tetraphase's possession and Control at such time, and (c) pursuant to, and under the terms of, a material transfer agreement to be mutually agreed by the Parties, the TP-6076 needed for Licensee to conduct China-strain minimum inhibitory concentration (MIC) testing of TP-6076 to support an IND filing in PRC for TP-6076, which testing shall be at Licensee's sole cost and expense ("**TP-6076 Data Package**"). Within [**] days after receipt of the complete TP-6076 Data Package, Licensee may provide written notice to Tetraphase of Licensee's interest in negotiating a license to Develop and Commercialize TP-6076 in the Territory (the "**TP-6076 Negotiation Notice**"); *provided* that Tetraphase shall respond to Licensee's inquiries with respect to TP-6076 (including with regard to the contents of the TP-6076 Data Package) during such [**] day exercise period, to the extent Tetraphase determines that such inquiries are reasonable. If Licensee provides such notice, the Parties shall enter into good faith negotiations with respect to such license, on such terms as may be mutually agreeable, which terms shall include Licensee sharing in the costs for any Tetraphase Entity's Phase 2 Clinical Trials of TP-6076 that supports registration in the Territory. If (a) Licensee does not provide the TP-6076 Negotiation Notice to Tetraphase within such [**] period or (b) Licensee provides the TP-6076 Negotiation Notice to Tetraphase during such [**] day period but the Parties are unable to reach mutual agreement and execute a definitive agreement with respect to the Development and Commercialization of TP-6076 in the Territory within [**] days from the date of the TP-6076 Negotiation Notice (or such extended period as may be approved in writing by the Parties) (**"Exclusive Negotiation Period"**), Licensee shall have no rights with respect to TP-6076. During the Exclusive Negotiation Period, Tetraphase shall neither license or otherwise grant to any Third Party, nor engage in any negotiations or other discussions with any Third Party regarding any agreement to license or otherwise grant to any Third Party, any rights to Develop and Commercialize TP-6076 in the Territory.

## ARTICLE III.

## GOVERNANCE

**Section 3.01 General.**

(a) The Parties shall establish (i) a Joint Steering Committee ("**JSC**") to oversee and coordinate the overall conduct of the Development and Commercialization of the Licensed Products in the Field in the Territory and (ii) a Joint Development Committee ("**JDC**") to oversee and coordinate the Development of the Licensed Products in the Field in the Territory. The JSC may, at the reasonable request of either Party, establish a Joint Commercialization Committee (" **JCC**") to oversee and coordinate the Commercialization of the Licensed Products in the Field in the Territory; *provided* that prior to any such establishment, any matters that would fall within the purview of the JCC pursuant to this **ARTICLE III (Governance)** shall instead fall within the purview of the JSC. The JSC, the JDC and the JCC shall each be referred to as a "**Committee**". Each Committee shall have decision-making authority with respect to the matters within its purview to the extent expressly provided herein.

(b) From time to time, each Committee may establish one or more subcommittees to oversee particular projects or activities, as it deems necessary or advisable (each, a "**Subcommittee**"). Each Subcommittee shall consist of such number of members as the applicable Committee determines is appropriate from time to time. Such members shall be individuals with expertise and responsibilities in the relevant areas. Such Subcommittees shall operate under the same principles as are set forth in this **ARTICLE III (Governance)** for the Committee forming such Subcommittee.

(c) At Tetraphase's written request, the Parties shall renegotiate this **ARTICLE III (Governance)** in good faith to include in the decision-making processes one or more Tetraphase Entities (other than Tetraphase) which are Developing or Commercializing the Licensed Compound or any Eravacycline Product outside of the Territory or Researching or Manufacturing the Licensed Compound or any Eravacycline Product; *provided* that such renegotiation shall not result in any alternative decision-making processes that would diminish Licensee's rights in any manner that may adversely impact Licensee's prospects with respect to the Development or Commercialization of any Licensed Product in any Jurisdiction in the Territory.

**Section 3.02 Joint Steering Committee.**

(a) Within [**] days following the Effective Date, the Parties shall establish the JSC. The JSC shall:

(i) manage the strategic direction of the Development and Commercialization of the Licensed Products in the Field in the Territory;

(ii) review and monitor the progress of the Development and Commercialization of the Licensed Products in the Field in the Territory and serve as a forum for exchanging information regarding the conduct of the Development and Commercialization of the Licensed Products in the Field in the Territory;

(iii) provide any information to Tetraphase that is necessary or reasonably useful for the Development or Commercialization of Eravacycline Products outside of the Territory;

(iv) oversee and coordinate all of the matters within the responsibilities of the Committees hereunder;

(v) serve as a forum for dispute resolution in accordance with **Section 3.07 (Committee Decision Making)** with respect to matters that are not resolved at the JDC and JCC; and

(vi) perform such other duties as are specifically assigned to the JSC under this Agreement.

**Section 3.03 Joint Development Committee.**

(a) Within [**] days following the Effective Date, the Parties shall establish the JDC. Upon the establishment of the JSC and the JDC, (i) each Party shall appoint the same [**] individuals to serve as such Party's representatives on the JSC and the JDC, and (ii) the JSC and JDC shall hold joint meetings, in each case ((i) or (ii)) until such time as either Party, in its sole discretion, determines it no longer desires the JSC and JDC to be so aligned. The JDC shall:

(i) review and approve the Development Plan and any proposed updates or amendments to the Development Plan, and propose revisions to the Development Plan in accordance with **Section 4.01 (Development in the Field in the Territory)**;

(ii) provide a forum for the Parties to share information with respect to the Development of the Licensed Products in the Field in the Territory, including reviewing and commenting on updates on such Development;

(iii) oversee, review, coordinate and provide strategic guidance to the Parties on the Development of the Licensed Products in the Field in the Territory;

(iv) subject to and within the parameters of the Development Plan (A) oversee the implementation of the Development Plan (including evaluation of clinical trial protocols and review of the conduct of clinical trials conducted pursuant to the Development Plan); and (B) oversee and approve the overall strategy and positioning of all material Regulatory Filings for Licensed Products in the Field in the Territory; and

(v) perform such other duties as are specifically assigned to the JDC under this Agreement.

**Section 3.04** **Joint Commercialization Committee.**

(a) At least [**] months prior to the anticipated filing of the first Drug Approval Application for a Licensed Product in the Field in the Territory, the JSC shall establish the JCC. The JCC shall:

(i) review and discuss the Launch Plan;

(ii) discuss implementation of the Launch Plan;

(iii) review and discuss the initial Commercialization Plan and, each year thereafter, review and approve the updated Commercialization Plan;

(iv) discuss implementation of the Commercialization Plan;

(v) review and discuss any branding and/or co-branding matters with respect to Licensed Products in the Field in the Territory; and

(vi) perform such other duties as are specifically assigned to the JCC under this Agreement.

**Section 3.05** **Membership**. Each Committee shall be composed of [**] representatives from each of Tetraphase and Licensee, each of which representatives shall be of the seniority and experience appropriate for service on the applicable Committee in light of the functions, responsibilities and authority of such Committee and the status of activities within the scope of the authority and responsibility of such Committee. Any representative from either Party can represent such Party on more than one Committee. Each Party may replace any of its representatives on any Committee at any time with prior written notice to the other Party; *provided* that such replacement meets the standard described in the preceding sentence. Each Party's representatives and any replacement of a representative shall be bound by obligations of confidentiality and non-use applicable to the other Party's Confidential Information that are at least as stringent as those set forth in **ARTICLE XII** (**Confidentiality**). Each Committee shall appoint a chairperson from among its members, with the first chairperson of each of the JSC and JDC being a representative of [**] and the first chairperson of the JCC being a representative of [**]. Each chairperson (whether initially appointed or any successor therefor) shall serve a term of one (1) year, at which time, the applicable Committee shall select a successor chairperson who is a representative of the Party other than the Party represented by the outgoing chairperson (*e.g.*, the second chairperson of each of the JSC and JDC shall be a representative of [**], and the second chairperson of the JCC shall be a representative of [**]; the third chairperson of each of the JSC and JDC shall be a representative of [**] and the third chairperson of the JCC shall be a representative of [**]). Within [**] days following each Committee meeting, the chairperson of the applicable Committee shall circulate to all Committee members a draft of the minutes of such meeting. The Committee shall then approve, by mutual agreement, such minutes within [**] days following circulation. No chairperson of any Committee shall have any greater authority than any other representative of such Committee.

**Section 3.06 Meetings.**

(a) Each Committee shall hold an initial meeting within [**] days after its formation or as otherwise agreed by the Parties. Thereafter, each Committee shall meet at least [**] following such Committee's formation, unless the respective Committee members otherwise agree. All Committee meetings may be conducted either by teleconference or, solely if agreed by the Parties, in person.

(b) Unless otherwise agreed by the Parties, the location at which in-person meetings for each Committee shall be held at the offices of Tetraphase, unless Licensee has offices in the United States, in which case, such meetings shall alternate between the offices of Tetraphase and the United States offices of Licensee. A reasonable number of other representatives of a Party, including, with respect to Tetraphase, any representative of any Tetraphase Entity that is Developing or Commercializing the Licensed Compound or any Eravacycline Product outside of the Territory or Researching or Manufacturing the Licensed Compound or any Licensed Product, may attend any Committee meeting as non-voting observers; *provided* that such additional representatives shall be bound by obligations of confidentiality and non-use applicable to the other Party's Confidential Information that are at least as stringent as those set forth in **ARTICLE XII (Confidentiality)**. Each Party shall be responsible for all of its own personnel and travel costs and expenses relating to participation in Committee meetings.

**Section 3.07 Committee Decision Making**. All decisions of a Committee shall be made by unanimous vote, with each Party's representatives collectively having one (1) vote, and shall be set forth in minutes approved by both Parties. Upon [**] Business Days prior written notice, either Party may convene a special meeting of a Committee for the purpose of resolving any failure to reach agreement on a matter within the scope of the authority and responsibility of such Committee. If the JDC or JCC is unable to reach agreement on any matter within [**] Business Days after the matter is referred to it or first considered by it, such matter shall be referred to the JSC for resolution. If the JSC is unable to reach agreement on any matter within [**] Business Days after the matter is referred to it or first considered by it, such matter shall be referred to the Executive Officers for resolution in accordance with **Section 3.08 (Executive Officers; Disputes)**.

**Section 3.08 Executive Officers; Disputes**. Each Party shall ensure that an executive officer is designated for such Party at all times during the Term for dispute resolution purposes (each such individual, such Party's "**Executive Officer**"), and shall promptly notify the other Party of its initial, or any change in its, Executive Officer. Unless otherwise set forth in this Agreement, in the event of a dispute arising under this Agreement between the Parties, the Parties shall refer such dispute to the Executive Officers, who shall attempt in good faith to resolve such dispute.

**Section 3.09 Final Decision-Making Authority**. If the Parties are unable to resolve a given dispute within the purview of a Committee within [**] Business Days after referring such dispute to the Executive Officers pursuant to **Section 3.08 (Executive Officers; Disputes)**, then, subject to **Section 3.10 (Limitations on Decision-Making)**:

(a) the Executive Officer of Tetraphase shall have the deciding vote on any matter that has any material adverse impact on the Development, Regulatory Approval process or Commercialization for any Eravacycline Product outside the Territory, including as a result of a material adverse impact on (i) the Research, Development or Commercialization of the Licensed Compound or any Eravacycline Product in any way outside the Territory or the Research or Manufacture of the Licensed Compound or any Eravacycline Product, (ii) the scope, validity or enforceability of any Tetraphase Technology or (iii) in Tetraphase's reasonable opinion, any In-License Agreement; and

(b) the Executive Officer of Licensee shall have the deciding vote on any matter solely related to the Development or Commercialization of Licensed Products in the Field in the Territory; *provided* that such matter does not fall under Tetraphase's final decision-making authority pursuant to **Section 3.09(a).**

Any decision made by an Executive Officer in accordance with this **Section 3.09 (Final Decision-Making Authority)** shall be deemed to be a decision of the relevant Committee.

**Section 3.10 Limitations on Decision-Making.**

(a) Neither Party shall have the deciding vote on, and no Committee shall have decision-making authority regarding, any of the following matters:

(i) the imposition of any requirements on the other Party to undertake obligations beyond those for which it is responsible, or to forgo any of its rights, under this Agreement;

(ii) the imposition of any requirements that the other Party takes or declines to take any action that would result in a violation of any Law or any agreement with any Third Party or the infringement of intellectual property rights of any Third Party;

(iii) the resolution of any dispute involving the breach or alleged breach of this Agreement;

(iv) any decision that is expressly stated to require the mutual agreement (or similar language) of the Parties or the approval of the other Party;

(v) any matters that would excuse such Party from any of its obligations under this Agreement; or

(vi) modifying the terms of this Agreement or taking any action to expand or narrow the responsibilities of any Committee.

(b) The decision-making Party shall make its decision in good faith, subject to the terms and conditions of this Agreement, and in a commercially reasonable manner without favoring other products being Developed, Manufactured or Commercialized by or on behalf of such Party or its Affiliates that are not Licensed Products.

(c) In no event may the decision-making Party unilaterally determine that it has fulfilled any obligations hereunder or that the non-deciding Party has breached any obligations hereunder.

(d) In no event may Licensee unilaterally determine that the events required for the payment of milestone payments have not occurred.

(e) In no event may Tetraphase unilaterally determine that the events required for the payment of milestone payments have occurred.

**Section 3.11** **Scope of Governance**. Notwithstanding the creation of each of the Committees, each Party shall retain the rights, powers and discretion granted to it under this Agreement, and no Committee shall be delegated or vested with rights, powers or discretion unless such delegation or vesting is expressly provided herein, or the Parties expressly so agree in writing. It is understood and agreed that issues to be formally decided by a particular Committee are only those specific issues that are expressly provided in this Agreement to be decided by such Committee, as applicable. For clarity, no Committee shall have any rights, powers or discretion to decide any matter not relating to the Development or Commercialization of the Licensed Product in the Field and the Territory, and Tetraphase retains all such rights, powers and discretion.

**Section 3.12** **Alliance Managers**. Each of the Parties shall appoint a single individual to manage Development, Manufacturing and Commercialization obligations between the Parties under this Agreement (each, an "**Alliance Manager**"). The role of the Alliance Manager is to act as a single point of contact between the Parties to ensure a successful relationship under this Agreement. The Alliance Managers may attend any Committee meetings. Each Alliance Manager shall be a non-voting participant in such Committee meetings, unless s/he is also appointed a member of such Committee; *provided, however*, that an Alliance Manager may bring any matter to the attention of a Committee if such Alliance Manager reasonably believes that such matter warrants such attention. Each Party may change its designated Alliance Manager at any time upon written notice to the other Party. Any Alliance Manager may designate a substitute to temporarily perform the functions of that Alliance Manager by written notice to the other Party. Each Party's Alliance Manager and any substitute for an Alliance Manager shall be bound by obligations of confidentiality and non-use applicable to the other Party's Confidential Information that are at least as stringent as those set forth in **ARTICLE XII** (**Confidentiality**). Each Alliance Manager will also: (a) plan and coordinate cooperative efforts and internal and external communications; and (b) facilitate the governance activities hereunder and the fulfillment of action items resulting from Committee meetings.

## ARTICLE IV.

## DEVELOPMENT

**Section 4.01 Development in the Field in the Territory.**

(a) The Development of Licensed Products in the Field in the Territory shall be governed by the Development Plan, and no Licensee Entity may Develop any Licensed Product in the Field in the Territory other than in accordance with the Development Plan, or as otherwise approved by Tetraphase in advance in writing. The initial framework for the Development Plan is attached to this Agreement as Exhibit B. The Parties shall, through the JDC, adopt the initial Development Plan within [**] days after the Effective Date, and once the JDC adopts such initial Development Plan it will be attached (or deemed attached) to this Agreement as Exhibit C. The JDC shall periodically review the Development Plan and determine whether to update the Development Plan. A Party may also develop and submit to the JDC from time to time proposed substantive amendments to the Development Plan. The JDC shall review such proposed amendments and may approve such proposed amendments or any other proposed amendments that the JDC may consider from time to time in its discretion and, upon any such approval by the JDC, the Development Plan shall be amended accordingly.

(b) If, at any time during the Term, Tetraphase notifies Licensee in writing that it plans to conduct, for any Licensed Product, a multi-region clinical trial that includes activities in the Territory, the Parties shall, subject to **Section 4.05 (Development Costs)**, amend the Development Plan to include such activities in the Territory, and Tetraphase shall grant to Licensee any rights required to enable Licensee to conduct such activities.

(c) Licensee shall use Commercially Reasonable Efforts to execute and to perform, or cause to be performed, the activities assigned to it in the Development Plan, in each case in accordance with **Section 4.03 (Standards of Conduct)**.

(d) Licensee shall use Commercially Reasonable Efforts to obtain, or cause to be obtained, Regulatory Approval and, if applicable, Reimbursement Approval, for a Licensed Product in the Field in each Jurisdiction in the Territory.

**Section 4.02 Development Reports**. Within [**] Business Days after the end of each calendar quarter, Licensee shall provide Tetraphase with a written report that summarizes the Development of the Licensed Products in the Field in the Territory performed by the Licensee Entities during the prior calendar quarter, which report shall include the status of each pending and proposed Regulatory Filing for Licensed Products in the Field in the Territory. In addition, Licensee shall promptly provide written notice to Tetraphase of any significant Development events (*e.g.*, any clinical trial initiation or completion, clinical holds, Regulatory Filings, Regulatory Approvals, Licensee Product Data).

**Section 4.03** **Standards of Conduct**. The Licensee Entities shall perform all Development activities under the Development Plan in a good scientific manner, in accordance with GLP and GCP, as applicable, and in compliance in all material respects with applicable Laws.

**Section 4.04** **Records**. The Licensee Entities shall maintain written or electronic records in sufficient detail, in a good scientific manner (in accordance with GLP and GCP, as applicable) and appropriate for regulatory and patent purposes, which are complete and accurate in all material respects and reflect all Development work performed under the Development Plan and results achieved. Tetraphase shall have the right, upon reasonable advance notice, and at reasonable intervals, to inspect and copy all such records (for clarity, including all applicable clinical, regulatory and quality records).

**Section 4.05** **Development Costs**. Except as expressly provided in this Agreement or the Development Plan, each Party shall bear its own costs incurred in the performance of its obligations under this **ARTICLE IV (Development)**. Notwithstanding the foregoing sentence, if any Tetraphase Entity, in collaboration with one or more Licensee Entities, conducts any multi-region clinical trial for any Licensed Product that includes any trial site in the Territory, Licensee may determine, at its sole discretion, whether to participate in such multi-region clinical trial. In the event that Licensee determines to participate in the aforementioned multi-region clinical trial, such trial shall enroll at least the minimum number of study subjects required to satisfy the applicable Regulatory Authority, and Licensee shall bear both (a) all costs incurred in the performance of such clinical trial in the Territory and (b) a *pro rata* portion of the Total Indirect Costs incurred in the performance of such multi-region clinical trial outside the Territory, which portion shall be the ratio of study sites in the Territory to total study sites worldwide, *provided* that such portion shall in no event exceed [**] percent ([**]%) of the Total Indirect Costs incurred in the performance of such multi-region clinical trial outside the Territory; *provided, however*, that (y) nothing in this Agreement shall prevent or delay any Tetraphase Entity from conducting any such multi-region clinical trial outside the Territory and (z) if Licensee determines not to participate in such multi-region clinical trial outside the Territory pursuant to **Section 4.05(b)**, then notwithstanding Licensee's rights pursuant to **Section 2.01(a)** and **Section 2.01(b)** or Licensee's access rights pursuant to **Section 2.04 (Knowledge Transfer)** or **Section 5.01(c)**, Licensee shall not have access to any Tetraphase Product Data or Tetraphase Regulatory Documents arising out of such multi-region clinical trial outside the Territory, unless and until Licensee pays to Tetraphase [**] percent ([**]%) of the amount provided pursuant to clauses (a) and (b) of this sentence with respect to such multi-region clinical trial.

## ARTICLE V.

## REGULATORY

**Section 5.01 Regulatory Filings.**

(a) Under the oversight of the JDC and subject to **Section 4.01(a)**, Licensee shall have the sole right to prepare, obtain, and maintain all Regulatory Filings and Regulatory Approvals, and to conduct communications with the Regulatory Authorities, for the Development or Commercialization of Licensed Products in the Field in the Territory. Licensee shall provide Tetraphase with an opportunity to review and comment on original language versions of all Regulatory Filings in the Territory for which Licensee is responsible under this **Section 5.01(a)**. Licensee shall provide access to interim drafts of all Regulatory Filings (in their original language) to Tetraphase via the access methods (such as secure databases) established by the JDC, and Tetraphase shall provide its comments on the final drafts of all Regulatory Filings or of proposed material actions within [**] days ([**] days for Drug Approval Applications), or such other longer period of time mutually agreed to by the Parties. In the event that a Regulatory Authority establishes a response deadline for any Regulatory Filing or material action shorter than such [**] day (or [**] day) period, the Parties shall work cooperatively to ensure the other Party has a reasonable opportunity for review and comment within such deadlines. Licensee shall, and shall cause relevant Licensee Entities to, consider any such comments from Tetraphase in good faith.

(b) All Regulatory Filings for Licensed Products in the Field in the Territory shall be filed in the name of Licensee or its designated Licensee Entity or designee, and all Licensee Regulatory Documents (including all Regulatory Approvals) shall be owned by, and shall be the sole property and held in the name of, Licensee or its designated Licensee Entity or designee. All Regulatory Filings and Regulatory Approvals in the Field in the Territory shall be at Licensee's sole expense.

(c) Subject to **Section 4.05(z)**, (i) Tetraphase shall, at Licensee's reasonable request and expense, provide Licensee with all reasonable assistance and support in obtaining Regulatory Approvals for the Licensed Products, and in the activities in support thereof, including providing necessary documents or other materials required by applicable Laws to obtain Regulatory Approvals, or attending meetings with Licensee and Regulatory Authorities relating to the Licensed Compound or a Licensed Product upon Licensee's request, in each case in accordance with the terms and conditions of this Agreement and the applicable Development Plan, and (ii) in support of Licensee's preparation and filing of any IND or Drug Approval Application with respect to any Licensed Product in the Field in the Territory, Tetraphase shall, at Licensee's reasonable written request and expense, provide Licensee a complete electronic copy of reasonably requested Tetraphase Regulatory Documents. In support of each Tetraphase Entity's preparation and filing of any IND or Drug Approval Application with respect to any Eravacycline Product outside of the Territory, at Tetraphase's reasonable written request, Licensee shall provide Tetraphase access to a complete electronic copy of all Licensee Regulatory Documents (in the original language).

## ARTICLE VI.

## COMMERCIALIZATION

**Section 6.01** **General**. Under the direction of the JCC, Licensee (itself or through any of the Licensee Entities) shall have the sole right to Commercialize the Licensed Products in the Field in the Territory at its own cost and expense (except as otherwise expressly set forth herein). At least [**] prior to anticipated filing of the first Drug Approval Application for a Licensed Product in the Field in the Territory, Licensee shall prepare a Launch Plan, which shall be reviewed by the JCC no later than [**] days after the JCC's receipt of such Launch Plan. Within [**] months prior to anticipated approval of the first Drug Approval Application for a Licensed Product in the Field in the Territory, Licensee shall prepare the initial Commercialization Plan, which shall be reviewed by the JCC no later than [**] days following the JCC's receipt of such Commercialization Plan. Each [**] thereafter, Licensee shall provide the JCC with an updated Commercialization Plan, which the JCC shall review and approve within [**] days after receipt thereof.

**Section 6.02** **Promotional Materials**. The Licensee Entities shall share their promotional materials for the Licensed Products with the JCC on a regular basis, and the JCC shall have the right to review and comment on, which comments shall be considered in good faith by Licensee, any of the Licensee Entities' promotional materials prior to their use in the Territory.

**Section 6.03** **Commercialization Reports**. Within [**] Business Days after the end of each calendar quarter following the First Commercial Sale of any Licensed Product in the Field in the Territory, Licensee shall provide the JCC with (i) a written report that summarizes Commercialization activities performed during the prior calendar quarter with respect to each Licensed Product in each Jurisdiction in the Territory, (ii) detailed sales reports for each month of the prior calendar quarter of each Licensed Product in each Jurisdiction in the Territory, and (iii) quarterly sales forecasts for each Licensed Product in each Jurisdiction in the Territory.

**Section 6.04** **Commercialization Efforts**. Licensee shall use Commercially Reasonable Efforts to Commercialize Licensed Products in the Field in the Territory following receipt of relevant Regulatory Approvals therefor.

**Section 6.05** **Standards of Conduct**. The Licensee Entities shall perform all Commercialization activities with respect to Licensed Products in the Field in the Territory in a professional and ethical business manner and in compliance in all material respects with applicable Laws.

**Section 6.06 Trademarks**.

(a) The applicable Tetraphase Entity(ies) shall own all rights to the Product Trademark(s) developed or used by the Tetraphase Entities with respect to the Commercialization of Licensed Products outside of the Territory (the "**Tetraphase Trademarks**"), and all goodwill associated therewith, in each country of the world. The applicable Tetraphase Entity(ies) shall also own rights to any Internet domain names incorporating any Tetraphase Trademark or any variation or part of any Tetraphase Trademark as its URL address or any part of such address. No Licensee Entity shall use any Tetraphase Trademark without Tetraphase's prior written consent.

(b) Licensee will develop and propose for the JCC's review and comment, which comments shall be considered in good faith by Licensee, one or more Product Trademark(s) for use by the Licensee Entities in the Field in the Territory. Any Product Trademark(s) (other than the Tetraphase Trademarks that Tetraphase permits Licensee to use) that are used by any Licensee Entity to Commercialize Licensed Products in the Field in the Territory are hereinafter referred to as the "**Licensee Trademarks**." The applicable Licensee Entity(ies) shall own all rights to Licensee Trademarks and all goodwill associated therewith, in each country of the world. The applicable Licensee Entity(ies) shall also own rights to any Internet domain name incorporating any Licensee Trademark or any variation or part of any Licensee Trademark as its URL address or any part of such address. No Tetraphase Entity shall use any Licensee Trademarks to Commercialize any Licensed Product without Licensee's prior written consent.

(c) Any use of Tetraphase's corporate name by any Licensee Entity shall require the prior written consent of Tetraphase.

(d) Except as expressly provided herein, or except as otherwise required by applicable Law or agreed by the Parties in advance in writing, neither Party shall have any right to use the other Party's or the other Party's Affiliates', and Licensee shall not have any right to use any Tetraphase Entity's, corporate names or logos in connection with any Development or Commercialization of any Licensed Product.

## ARTICLE VII.

## MANUFACTURE AND SUPPLY

**Section 7.01** **Supply Obligations**. From and after the execution of applicable Supply Agreements pursuant to **Section 7.02 (Supply Agreement)**, and subject to the terms of such Supply Agreements, Tetraphase will use Commercially Reasonable Efforts, either itself or through Third Parties, to Manufacture Finished Drug Product and supply to Licensee Finished Drug Product in quantities that are reasonably sufficient for the conduct of Development and Commercialization of Licensed Products in the Field in the Territory by the Licensee Entities. For any Finished Drug Product supplied by Tetraphase to Licensee pursuant to this **Section 7.01 (Supply Obligations)** for purposes of Commercialization of Licensed Products in the Field in the Territory, Licensee shall pay to Tetraphase an amount equal to [**] percent ([**]%) of Tetraphase's COGS for such Finished Drug Product, payable within [**] days after receipt of an invoice therefor. For any Finished Drug Product supplied by Tetraphase to Licensee pursuant to this **Section 7.01 (Supply Obligations)** for purposes of Development of Licensed Products in the Field in the Territory, Licensee shall pay to Tetraphase an amount equal to [**] percent ([**]%) of Tetraphase's COGS for such Finished Drug Product, payable within [**] days after receipt of an invoice therefor.

**Section 7.02** **Supply Agreements**. Within [**] days after the Effective Date, or at such later date as may be mutually agreed in writing, the Parties will negotiate in good faith and enter into one or more supply agreements for clinical (including investigator-sponsored trials, but solely to the extent such investigator-sponsored trials have been mutually approved by both Parties) and commercial supply of Licensed Products and related quality agreement(s) (collectively, the "**Supply Agreements**"), which Supply Agreements will be consistent with the terms set forth in **Section 7.01 (Supply Obligations)**. In addition, the Supply Agreements shall include a provision for the Parties to negotiate in good faith, for a reasonable period of time at the relevant point during which Tetraphase is providing clinical supply to Licensee, the terms and conditions on which Tetraphase would transfer to Licensee or a Third Party manufacturer approved by Tetraphase the then-current process for the Manufacture of the Licensed Products and grant Licensee the right to Manufacture, or have Manufactured, the Licensed Product for Commercialization of the Licensed Product in the Field in the Territory, including, to the extent required, amendment of the relevant provisions of this Agreement to such grant of rights, including **Sections 1.71, 1.72, 1.73, 2.01 and 2.06(a)(ii)**. Notwithstanding anything to the contrary set forth herein, when the Parties enter into the Supply Agreements, the terms of such Supply Agreements shall supersede the terms set forth in **Section 7.01 (Supply Obligations)** and in this **Section 7.02 (Supply Agreement)**.

## ARTICLE VIII.

## PAYMENTS

**Section 8.01** **Upfront Payment**. Within [**] Business Days after the Effective Date, Licensee shall pay Tetraphase a one-time, non-refundable, non-creditable upfront payment of Seven Million Dollars ($7,000,000).

**Section 8.02** **Development Milestone Payment.**

(a) Licensee shall make the non-refundable, non-creditable milestone payments to Tetraphase set forth in the table below, each payable once only, no later than [**] days after the earliest date on which the corresponding milestone event has first been achieved by any Licensee Entity with respect to the first Licensed Product to achieve such milestone event.

| Milestone Event | Milestone Payment |
|---|---|
| [**] | [**] |
| [**] | [**] |
| [**] | [**] |
| [**] | [**] |

(b) If Licensee has not paid to Tetraphase a milestone payment set forth in a row in the table in **Section 8.02(a)**, and a milestone event set forth in a later row in the table in **Section 8.02(a)** occurs, then, upon the occurrence of such milestone event set forth in such later row, Licensee shall pay to Tetraphase the milestone payment set forth in such earlier row. By way of example and not limitation, if Licensee has not paid to Tetraphase the milestone payment set forth in row (a)(i), and the milestone event set forth in row (a)(ii), (a)(iii) or (a)(iv) occurs, then, upon such event, Licensee shall pay to Tetraphase the milestone payment set forth in row (a)(i).

(c) Upon achievement by any Licensee Entity of any of the milestone events listed above, Licensee shall promptly (but in no event more than [**] days after such achievement) notify Tetraphase of such achievement.

**Section 8.03** **Sales Milestone Payments**. Licensee shall pay to Tetraphase the following non-refundable and non-creditable amounts after the first achievement of aggregate Net Sales of all Licensed Products in the Territory in a calendar year that meet or exceed the minimum annual Net Sales thresholds set forth below, which payment shall be made no later than [**] days after the end of such calendar year:

| Annual Net Sales Threshold | Payment Amount |
|---|---|
| Equal to or greater than $[**] | [**] |
| Equal to or greater than $[**] | [**] |
| Equal to or greater than $[**] | [**] |

Each milestone payment in this **Section 8.03 (Sales Milestone Payments)** shall be payable only once upon the first achievement of such milestone in a given calendar year and no amounts shall be due for subsequent or repeated achievements of such milestone in subsequent calendar years. For clarity, the Net Sales of all Licensed Products in a calendar year shall be aggregated for purposes of determining whether any milestone in the table above has been met. If more than one of the milestones set forth in the table above are first achieved in a single calendar year, then Licensee shall pay to Tetraphase in such calendar year all of the payments corresponding to all of the milestones achieved in such calendar year under this **Section 8.03 (Sales Milestone Payments)**.

**Section 8.04 Royalties.**

(a) Subject to the remainder of this **Section 8.04 (Royalties)**, Licensee shall pay Tetraphase the following royalties on aggregate Net Sales of all Licensed Products, at an incremental royalty rate determined by aggregate annual Net Sales of all Licensed Products in each calendar year during the Term in the Territory:

| **Portion of Annual Net Sales of all Licensed Products** | **Royalty** |
|---|---|
| Less than or equal to $[**] | [**] |
| Greater than $[**] and less than or equal to $[**] | [**] |
| Greater than $[**] | [**] |

By way of example and not limitation, if Net Sales of all Licensed Products in the first quarter of a calendar year are [**] Dollars ($[**]), then the royalty shall be [**].

(b) Running royalties paid by Licensee under this **Section 8.04** (**Royalties**) shall be paid on a Licensed Product-by-Licensed Product and Jurisdiction-by-Jurisdiction basis until the latest of (i) expiration of the last-to-expire Valid Claim that is a composition of matter claim (for clarity, including a formulation claim) in the Tetraphase Patent Rights or Joint Patent Rights that Covers such Licensed Product in the Field in such Jurisdiction, (ii) expiration of marketing or regulatory exclusivity with respect to such Licensed Product in such Jurisdiction, or (iii) ten (10) years from the First Commercial Sale of such Licensed Product in the Field in such Jurisdiction (each, a "**Royalty Term**"). Following the expiration of the Royalty Term with respect to a particular Licensed Product in the Field in a Jurisdiction, the license granted by Tetraphase to Licensee pursuant to **Section 2.01(a)** with respect to such Licensed Product in the Field in such Jurisdiction shall be perpetual, irrevocable, fully-paid and royalty-free, and Net Sales of such Licensed Product shall no longer be included in the aggregate Net Sales calculation in **Section 8.03 (Sales Milestone Payments)** or **Section 8.04(a)**.

(c) Notwithstanding the foregoing, in the event that, on a Licensed Product-by-Licensed Product, Jurisdiction-by-Jurisdiction and (subject to **Section 8.04(c)(iv)**) calendar quarter-by-calendar quarter basis:

(i) in such Jurisdiction in the Territory during such calendar quarter during the Royalty Term for such Licensed Product, one or more applicable Generic Products are on the market in such Jurisdiction and unit sales of such Generic Product(s) in such Jurisdiction constitute more than [**] percent ([**]%) but less than [**] percent ([**]%) of the total unit sales of such Generic Product(s) and Licensed Product in such Jurisdiction, Licensee shall, for such calendar quarter for such Licensed Product in such Jurisdiction, pay to Tetraphase a royalty rate that is [**] percent ([**]%) of the applicable rate set forth in **Section 8.04(a)**;

(ii) in such Jurisdiction in the Territory during such calendar quarter during the Royalty Term for such Licensed Product, one or more applicable Generic Products are on the market in such Jurisdiction and unit sales of such Generic Product(s) in such Jurisdiction constitute [**] percent ([**]%) or more of the total unit sales of such Generic Product(s) and Licensed Product in such Jurisdiction, Licensee shall, for such calendar quarter for such Licensed Product in such Jurisdiction, pay to Tetraphase a royalty rate that is [**] percent ([**]%) of the applicable rate set forth in **Section 8.04(a)**;

**(iii)** in the event that **Section 8.04(c)(i)**, **Section 8.04(c)(ii)** does not apply, but, under applicable Law, the royalty rate must be reduced in order to ensure enforceability of the royalty obligation once clause (i) or (ii) of the Royalty Term ends with respect to a Licensed Product in a Jurisdiction, then the royalty with respect to such Licensed Product in such Jurisdiction shall be reduced by [**] percent ([**]%) from the rate set forth in **Section 8.04(a)**.

**(iv)** Subject in all cases to **Section 8.04(d)**, if (A) a royalty reduction pursuant to **Section 8.04(c)(i)** or **Section 8.04(c)(ii)** is applicable with respect to a calendar quarter, (B) Licensee has paid to Tetraphase a royalty payment with respect to such calendar quarter pursuant to **Section 8.05 (Royalty Payments and Reports)** and (C) any or all of the amount of royalty reduction to which Licensee is entitled as set forth in clause (A) of this sentence was not applied to the royalty payment paid as set forth in clause (B) of this sentence due to time lag of information regarding market share of Generic Product(s), then the amount of reduction not applied shall be fully creditable against payments owed by Licensee to Tetraphase in one or more subsequent calendar quarters.

(d) On a Licensed Product-by-Licensed Product, Jurisdiction-by-Jurisdiction and calendar quarter-by-calendar quarter basis, in no event shall the royalty rate payable to Tetraphase under this **Section 8.04 (Royalties)** be reduced by more than [**] percent ([**]%) of what it would otherwise be by operation of **Section 8.04(a)** alone with respect to such Licensed Product in such Jurisdiction in such calendar quarter as a result of the reductions set forth in **Section 8.04(c)**.

**Section 8.05 Royalty Payments and Reports.**

(a) On a Licensed Product-by-Licensed Product and Jurisdiction-by-Jurisdiction basis, until the expiration of the Royalty Term with respect to such Licensed Product in such Jurisdiction, Licensee agrees to provide (i) written reports to Tetraphase within [**] Business Days after the end of each calendar month providing a good faith estimate of Net Sales of such Licensed Product in such Jurisdiction by any Licensee Entity in such calendar month and (ii) quarterly written reports to Tetraphase within [**] Business Days after the end of each

calendar quarter, covering all Net Sales of such Licensed Product in such Jurisdiction by any Licensee Entity, each such written report under this clause (ii) stating for the period in question (A) the amount of gross sales and Net Sales of each Licensed Product in each Jurisdiction in the Territory during the applicable calendar quarter (including such amounts expressed in local currency and as converted to Dollars) and a calculation of the amount of royalty payment due on such Net Sales for such calendar quarter and (B) such information as is reasonably necessary for Tetraphase to comply with its reporting obligations under Section 7.1.1 of the Harvard Agreement.

(b) Licensee shall make the royalty payments due hereunder within [**] days after the end of each calendar quarter.

**Section 8.06** **Financial Responsibility for In-License Agreements.** Provided that Licensee has complied with this Agreement, Tetraphase shall be solely responsible for payment of any and all amounts due to any Third Party counterparty under or in connection with any In-License Agreement except as set forth in **Section 9.04(a)(i)** and **Section 9.05(c)(i)**. Licensee shall be solely responsible for payment of any and all amounts due to any Third Party under or in connection with any Licensee In-License Agreement.

**Section 8.07** **Accounting.** Each Licensee Entity shall keep full, clear and accurate records of Licensed Products that are made, used or sold under this Agreement, in accordance with the Accounting Standards consistently applied, for a period of at least [**] years after the end of the calendar year to which the records relate, setting forth the sales of Licensed Products in sufficient detail to enable royalties and other amounts payable to Tetraphase hereunder to be determined. Each Licensee Entity further agrees to permit its books and records to be examined by an independent accounting firm selected by Tetraphase or Harvard, as applicable, and reasonably acceptable to Licensee, to verify any reports and payments delivered under this Agreement, upon reasonable notice (which shall be no less than [**] days prior notice) and during regular business hours and subject to a reasonable confidentiality agreement. The Parties shall reconcile any underpayment or overpayment within [**] days after the accounting firm delivers the results of any audit. Such examination is to be made at the expense of Tetraphase or Harvard, as applicable, except in the event that the results of the audit reveal an underpayment by Licensee of [**] percent ([**]%) or more during the period being audited, in which case reasonable audit fees for such examination shall be paid by Licensee.

**Section 8.08** **Currency Conversion.** Wherever it is necessary to convert currencies for Net Sales invoiced in a currency other than the Dollar, such conversion shall be made into Dollars at the conversion rate existing in the United States (as reported in the *Wall Street Journal*) on the last working day of the applicable calendar quarter or, if such rate is unavailable, a substitute therefor reasonably selected by Tetraphase. All payments due to Tetraphase under this Agreement shall be made without deduction of exchange, collection or other charges.

**Section 8.09** **Methods of Payment**. All payments due to Tetraphase under this Agreement shall be made in Dollars by wire transfer to a bank account of Tetraphase designated from time to time in writing by Tetraphase.

**Section 8.10** **Taxes**.

(a) Licensee Entities will make all payments to Tetraphase under this Agreement without deduction or withholding for Taxes except to the extent that any such deduction or withholding is required by applicable Law in effect at the time of payment.

(b) The full amount of any Tax required to be deducted or withheld within the meaning of **Section 8.10(a)** on payments under this Agreement will be duly deducted, withheld and timely paid over by Licensee Entities on behalf of Tetraphase. If, in accordance with the foregoing, a Licensee Entity withholds any amount, it shall pay to Tetraphase the balance when due, make timely payment to the proper Governmental Authority of the withheld amount and send to Tetraphase proof of such payment within [**] days following such payment.

(c) The Parties will cooperate with respect to all documentation required by any taxing authority or reasonably requested by either Party to secure a reduction in the rate of applicable withholding Taxes.

(d) If (i) a Licensee Entity (A) had a duty to deduct, withhold and pay over any Tax to any Governmental Authority in connection with any payment it made to Tetraphase under this Agreement but (B) failed to so deduct, withhold and timely pay over all or any portion of such Tax, and (ii) such Tax or portion thereof is assessed against Tetraphase, then such Licensee Entity will indemnify and hold harmless Tetraphase from and against any penalties imposed as a result thereof.

(e) To the extent any VAT is due on any amounts payable to Tetraphase under this Agreement, the applicable Licensee Entity shall bear and timely pay such VAT. The Parties will cooperate to provide Licensee Entity all documentation required to properly and timely pay such VAT.

(f) For example, if a Licensee Entity is required by the terms and conditions of this Agreement, prior to operation of this **Section 8.10 (Taxes)**, to make a payment of [**] Dollars ($[**]) to Tetraphase, and such payment is subject to [**] percent ([**]%) PRC tax withholding and [**] percent ([**]%) VAT, Licensee shall (i) deduct such [**] percent ([**]%) tax withholding and pay to Tetraphase [**] Dollars ($[**]) and (ii) be responsible for such [**] percent ([**]%) VAT and pay to the applicable Governmental Authority [**] Dollars ($[**]).

**Section 8.11** **Late Payments**. Interest shall be payable by Licensee on any amounts payable to Tetraphase under this Agreement which are not paid by the due date for payment. All interest shall accrue and be calculated on a daily basis (both before and after any judgment) at a rate per month equal to the lesser of (a) the higher of (i) [**] above the then-current "prime rate" in effect published in *The Wall Street Journal* or (ii) [**] percent ([**]%) per month or (b) the maximum rate permissible under applicable Law, for the period from the due date for payment until the date of actual payment. The payment of such interest shall not limit Tetraphase from exercising any other rights it may have as a consequence of the lateness of any payment.

## ARTICLE IX.

## OWNERSHIP OF INTELLECTUAL PROPERTY

**Section 9.01** **Tetraphase Intellectual Property**. Ownership of the Tetraphase Technology shall remain vested at all times in Tetraphase.

**Section 9.02** **Licensee Intellectual Property**. Ownership of the Licensee Technology shall remain vested at all times in Licensee.

**Section 9.03** **Joint Technology.**

(a) Each Party shall promptly disclose to the other Party any Joint Invention upon becoming aware thereof, but in any event no later than [**] days after the identification, conception, discovery, authorship, development or reduction to practice thereof.

(b) Ownership of Joint Technology shall be vested jointly in Tetraphase and Licensee. For purposes of determination of ownership hereunder, inventorship shall be determined according to United States patent Laws.

**Section 9.04** **Prosecution of Patent Rights.**

(a) Subject to the terms of each In-License Agreement:

(i) Tetraphase shall have the sole right, but not the obligation, to file, prosecute and maintain all Tetraphase Patent Rights that are licensed to Tetraphase under the Harvard Agreement (the "**Harvard Patent Rights**") and the first right, but not the obligation, to file, prosecute and maintain all other Tetraphase Patent Rights and all Joint Patent Rights. Licensee shall reimburse Tetraphase for (i) all costs incurred by Tetraphase after the Effective Date in filing, prosecuting and maintaining Tetraphase Patent Rights (for the avoidance of doubt, including amounts paid by Tetraphase after the Effective Date to any Third Party counterparty under any In-License Agreement, including amounts paid after the Effective Date to Harvard under Section 3.3 of the Harvard Agreement, with respect to such Third Party counterparty's filing, prosecution and maintenance of applicable Tetraphase Patent Rights), (ii) all costs incurred by Tetraphase in filing, prosecuting and maintaining Joint Patent Rights that Cover Licensed Products in the Field in the Territory and (iii) [**] percent ([**]%) of all costs incurred by Tetraphase in filing, prosecuting and maintaining all other Joint Patent Rights, in each case ((i)-(iii)) within [**] days after receiving an invoice therefor.

(ii) Tetraphase shall consult with Licensee on the preparation, filing, prosecution and maintenance of all Tetraphase Patent Rights and Joint Patent Rights, and shall take into consideration the commercial strategy of Licensee in the Territory. Tetraphase shall furnish Licensee with copies of each document relevant to such preparation, filing, prosecution and maintenance at least [**] days prior to filing such document or making any payment due thereunder to allow for review and comment by Licensee and shall consider in good faith timely comments from Licensee thereon; *provided* that any comment provided by Licensee with [**] days of Licensee's receipt of the applicable document shall be considered "timely" for purposes of this sentence. Tetraphase shall also furnish Licensee with copies of all final filings and

responses made to any patent authority with respect to the Tetraphase Patent Rights and Joint Patent Rights in a timely manner following submission thereof.

(iii) Licensee shall, without cost to Tetraphase, obtain all necessary assignment documents for Tetraphase, render all signatures that shall be necessary for the relevant patent filings and assist Tetraphase in all other reasonable ways that are necessary for the filing, prosecution, issuance and maintenance of the Joint Patent Rights.

(iv) Should Tetraphase decide that it is no longer interested in maintaining or prosecuting a particular Tetraphase Patent Right (other than a Harvard Patent Right) or Joint Patent Right during the Term, it shall promptly provide Licensee written notice of this decision. Absent such written notice to Licensee, Tetraphase shall use commercially reasonable efforts to file, prosecute and maintain all Tetraphase Patent Rights (other than Harvard Patent Rights) and all Joint Patent Rights that Cover Licensed Products in the Field in the Territory. Licensee may, upon written notice to Tetraphase, assume such prosecution and maintenance at Licensee's sole expense.

(b) Subject to the terms of each Licensee In-License Agreement:

(i) Licensee shall have the sole right, but not the obligation, to file, prosecute and maintain all Licensee Patent Rights that Cover Licensed Products in the Field in the Territory, and the first right, but not the obligation, to file, prosecute and maintain all other Licensee Patent Rights. Licensee agrees to use commercially reasonable efforts to file, prosecute and maintain all Licensee Patent Rights that Cover Licensed Products in the Territory.

(ii) Licensee shall consult with Tetraphase on the preparation, filing, prosecution and maintenance of all Licensee Patent Rights shall furnish Tetraphase with copies of each document relevant to such preparation, filing, prosecution and maintenance at least [**] days prior to filing such document or making any payment due thereunder to allow for review and comment by Tetraphase and shall consider in good faith timely comments from Tetraphase thereon; *provided* that any comment provided by Tetraphase with [**] days of Tetraphase's receipt of the applicable document shall be considered "timely" for purposes of this sentence. Licensee shall also furnish Tetraphase with copies of all final filings and responses made to any patent authority with respect to the Licensee Patent Rights in a timely manner following submission thereof.

**Section 9.05** **Enforcement and Defense.** Subject to the terms of each In-License Agreement:

(a) If either Party becomes aware of any Third Party activity in the Territory, including any Development activity (whether or not an exemption from infringement liability for such Development activity is available under applicable Law), that infringes (or that is directed to the Development of a product that would infringe) a Tetraphase Patent Right or a Joint Patent Right, or that misappropriates any Tetraphase Know-How or Joint Know-How, then the Party becoming aware of such activity shall give prompt written notice to the other Party regarding such alleged infringement or misappropriation (collectively, "**Infringement Activity**").

(b) Tetraphase shall have the first right, but not the obligation, to attempt to resolve any Infringement Activity by commercially appropriate steps at its own expense, including the filing of an infringement or misappropriation suit using counsel of its own choice. If Tetraphase fails to resolve such Infringement Activity or to initiate a suit with respect thereto by the date that is [**] days before any deadline for taking action to avoid any loss of material enforcement rights or remedies, then, with Tetraphase's written consent (which shall not be unreasonably withheld, conditioned or delayed), Licensee shall have the right, but not the obligation, to attempt to resolve such Infringement Activity by commercially appropriate steps at its own expense, including the filing of an infringement or misappropriation suit using counsel of its own choice.

(c) Any amounts recovered by a Party as a result of an action pursuant to **Section 9.05(b)**, whether by settlement or judgment, shall be allocated as follows:

(i) first, the Parties shall pay to each Third Party counterparty under any In-License Agreement any amounts owed to such Third Party counterparty with respect to such enforcement action, including any amounts owed to Harvard pursuant to Section 8.2 or 8.3 of the Harvard Agreement;

(ii) second, each Party's internal and external costs associated with the enforcement action shall be reimbursed; and

(iii) third, any remaining amount shall be retained [**] percent ([**]%) by the enforcing Party and paid [**] percent ([**]%) to the other Party.

(d) In any event, at the request and expense of the Party bringing an infringement or misappropriation action under **Section 9.05(b)**, the other Party shall provide reasonable assistance in any such action (including entering into a common interest agreement if reasonably deemed necessary by any Party) and to be joined as a party to the suit if necessary for the initiating Party to bring or continue such suit. Neither Party may settle any action or proceeding brought under **Section 9.05(b)**, or knowingly take any other action in the course thereof, in a manner that materially adversely affects the other Party's interest in any Tetraphase Patent Rights or Joint Patent Rights without the written consent of such other Party. Each Party shall always have the right to be represented by counsel of its own selection and its own expense in any suit or other action instituted by the other Party pursuant to **Section 9.05(b)**.

(e) If a Third Party asserts that a Tetraphase Patent Right (other than a Harvard Patent Right) or Joint Patent Right in mainland China is invalid or unenforceable, then Licensee shall have the first right, but not the obligation, to defend against such assertion and, at Licensee's request and expense, Tetraphase shall provide reasonable assistance in defending against such Third Party assertion. Licensee shall (i) keep Tetraphase reasonably informed regarding such assertion and such defense (including by providing Tetraphase with drafts of each filing a reasonable period before the deadline for such filing and promptly providing Tetraphase with copies of all final filings and correspondence), (ii) consult with Tetraphase on such defense, and (iii) consider in good faith all comments from Licensee regarding such defense. In the event Licensee controls such defense, Tetraphase shall have the right to join as a party to such defense and participate with its own counsel at its sole cost; *provided* that Licensee shall retain control of

such defense. Should Licensee decide that it is not, or is no longer, interested in controlling such defense, it shall promptly (and in any event by the date that is [**] days before any deadline for taking action to avoid any loss of material rights) provide Tetraphase written notice of this decision. Tetraphase may, upon written notice to Licensee, assume such defense at Tetraphase's sole expense.

(f) If a Third Party asserts that a Tetraphase Patent Right or Joint Patent Right anywhere in the Territory other than in mainland China is invalid or unenforceable, then Tetraphase shall have the first right, but not the obligation, to defend against such assertion. Should Tetraphase decide that it is not, or is no longer, interested in controlling such defense with respect to any Tetraphase Patent Right other than a Harvard Patent Right or any Joint Patent Right, it shall promptly (and in any event by the date that is [**] days before any deadline for taking action to avoid any loss of material rights) provide Licensee written notice of this decision. Licensee may, upon written notice to Tetraphase, assume such defense at Licensee's sole expense.

**Section 9.06** **Defense of Third Party Infringement and Misappropriation Claims.** Subject to the terms of each In-License Agreement:

(a) If a Third Party asserts that a Patent Right or other right controlled by it in the Territory is infringed or misappropriated by a Party's activities under this Agreement or a Party becomes aware of a Patent Right or other right that might form the basis for such a claim, the Party first obtaining knowledge of such a claim or such potential claim shall immediately provide the other Party with notice thereof and the related facts in reasonable detail. The Parties shall discuss what commercially appropriate steps, if any, to take to avoid infringement or misappropriation of said Third Party Patent Right or other right controlled by such Third Party in the Territory.

(b) If a Third Party asserts that a Patent Right or other right controlled by it in the Territory is infringed or misappropriated by a Party's activities under this Agreement, then such Party shall have the first right, but not the obligation, to defend against such assertion and, at such Party's request and expense, the other Party will provide reasonable assistance in defending against such Third Party assertion. Such Party shall keep the other Party reasonably informed regarding such assertion and such defense.

**Section 9.07** **Patent Term Extensions**. Subject to the terms of each In-License Agreement, Tetraphase shall have the sole authority to select the appropriate Tetraphase Patent Rights or Joint Patent Rights for filing to obtain patent term extensions, including supplementary protection certificates and any other extensions that are now available or become available in the future, for Licensed Products in the Field in the Territory, and shall consult with Licensee with respect to such decisions and shall consider the comments and concerns of Licensee in good faith. Licensee shall cooperate with Tetraphase in gaining any such patent term extensions, including by signing all necessary papers.

**Section 9.08** **Trademarks**. Licensee shall be responsible for the registration, maintenance and enforcement of the Licensee Trademarks throughout the Territory, as well as all expenses associated therewith.

**Section 9.09** **Recordal**. Tetraphase shall, at Licensee's request and expense, promptly provide Licensee with all necessary assistance and documents required for all government approvals, registrations and/or recordals required or advisable under any applicable Law in the Territory (or any part thereof) to enable the Parties to exercise, enforce and enjoy all of the rights and obligations contained thereunder, including any approval, registration or recordal required under the People's Republic of China ("**PRC**") technology import and export laws and the PRC patent laws.

## ARTICLE X.

## DATA SECURITY AND ADVERSE DRUG EVENTS AND REPORTS

**Section 10.01** **Data Security**. During the Term, Tetraphase and its Affiliates and each Licensee Entity will maintain safety and facility procedures, data security procedures and other safeguards against the disclosure, destruction, loss, or alteration of Licensee's or Tetraphase's, respectively, information in its possession, which such procedures and safeguards shall be no less rigorous than those maintained by Tetraphase or Licensee, respectively, for its own information of a similar nature.

**Section 10.02** **Complaints**. Each Party shall maintain a record of all non-medical and medical product-related complaints it receives with respect to the Licensed Compound or any Licensed Product. Each Party shall notify the other Party of any such complaint received by it in sufficient detail and in accordance with the timeframes and procedures for reporting established, and in any event in sufficient time to allow each Tetraphase Entity and each Licensee Entity to comply with any and all regulatory requirements imposed upon it, including in accordance with International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use ("**ICH**") guidelines. The Party that holds the applicable Regulatory Filing(s) in a particular country shall investigate and respond to all such complaints in such country with respect to the Licensed Compound or any Licensed Product as soon as reasonably practicable. All such responses shall be made in accordance with the procedures established pursuant to ICH, FDA, EMA, CFDA and other applicable guidelines. The Party responsible for responding to such complaint shall promptly provide the other Party a copy of any such response.

**Section 10.03** **Adverse Drug Events.** [**] days prior to the commencement of any clinical trial for any Licensed Product in the Territory, the Parties shall enter into the Safety Data Exchange Agreement. Such Safety Data Exchange Agreement shall provide for the exchange by the Parties of any information of which a Party becomes aware concerning any adverse event experienced by a subject or patient being administered any Licensed Product, whether or not such adverse event is determined to be attributable to any Licensed Product, including any such information received by either Party from any Third Party (subject to receipt of any required consents from such Third Party). It is understood that each Party and its Affiliates and licensees or sublicensees shall have the right to disclose such information if such disclosure is reasonably necessary to comply with applicable Laws and requirements of any applicable Regulatory Authority. The Safety Data Exchange Agreement will also detail Licensee's responsibilities relating to recalls, suspensions and withdrawals of each Licensed Product.

## ARTICLE XI.

## REPRESENTATIONS, WARRANTIES, AND COVENANTS

**Section 11.01** **Mutual Representations and Warranties**. Each of Licensee and Tetraphase hereby represents and warrants to the other Party as of the Effective Date that:

(a) it is a corporation or entity duly organized and validly existing under the Laws of the state, municipality, province, administrative division or other jurisdiction of its incorporation or formation;

(b) the execution, delivery and performance of this Agreement by it has been duly authorized by all requisite corporate action;

(c) it has the power and authority to execute and deliver this Agreement and to perform its obligations hereunder, and such performance does not conflict with or constitute a breach of any of its agreements with any Third Party;

(d) it has the right to grant the rights and licenses described in this Agreement;

(e) it has not made any commitment to any Third Party in conflict with the rights granted by it hereunder;

(f) to its knowledge, no consent, approval or agreement of any person or Governmental Authority is required to be obtained in connection with the execution and delivery of this Agreement; and

(g) it has not been debarred by the FDA, is not the subject of a conviction described in Section 306 of the FD&C Act, and is not subject to any similar sanction of a other Governmental Authority outside of the U.S., and neither it nor any of its Affiliates has used, in any capacity, any person who either has been debarred by the FDA, is the subject of a conviction described in Section 306 of the FD&C Act or is subject to any such similar sanction inside or outside of the U.S.

**Section 11.02** **Mutual Covenants**. Each of Licensee and Tetraphase hereby covenants to the other Party that:

(a) it will not engage, in any capacity in connection with this Agreement or any ancillary agreement, any person who either has been debarred by the FDA, is the subject of a conviction described in Section 306 of the FD&C Act or is subject to any such similar sanction inside or outside of the U.S., and such Party shall inform the other Party in writing promptly if such Party or any person engaged by such Party who is performing services under this Agreement, or any ancillary agreements, is debarred or is the subject of a conviction described in Section 306 of the FD&C Act or any similar sanction inside or outside of the U.S., or if any action, suit, claim, investigation or legal or administrative proceeding is pending or, to such Party's knowledge, is threatened, relating to the debarment or conviction of a Party, any of its Affiliates or any such person performing services hereunder or thereunder;

(b) during the Term, it will not make any commitment to any Third Party in conflict with the rights granted by it hereunder; and

(c) it will comply with all applicable Laws in performing its activities hereunder.

**Section 11.03** **Additional Tetraphase Warranties**. Tetraphase hereby represents and warrants to Licensee as of the Effective Date that:

(a) to Tetraphase's knowledge, Exhibit A contains a list of all Tetraphase Patent Rights existing as of the Effective Date (the "**Existing Patents**");

(b) to Tetraphase's knowledge, each issued patent within the Existing Patents as of the Effective Date is not invalid or unenforceable, in whole or in part;

(c) all of the In-License Agreements existing on the Effective Date are listed on Exhibit E;

(d) there are no claims, judgments, or settlements against, or amounts with respect thereto, owed by Tetraphase or any of its Affiliates relating to the Existing Regulatory Documents, the Existing Patents, or the Tetraphase Know-How;

(e) no claim or litigation has been brought and served on Tetraphase, or, to Tetraphase's knowledge, threatened, by any Person alleging that the issued patents in the Existing Patents are invalid or unenforceable;

(f) to Tetraphase's knowledge, the Development or Commercialization in the Territory of the Licensed Product, in the intravenous form in which such Licensed Product is being clinically Developed by Tetraphase in the U.S. as of the Effective Date and in the indications for which such form has been clinically Developed by Tetraphase in the U.S. as of the Effective Date, will not infringe any Patent Right;

(g) to Tetraphase's knowledge, no Third Party is infringing or misappropriating any Tetraphase Technology in the Field in the Territory in derogation of the rights granted to Licensee in this Agreement;

(h) Tetraphase has not received written notice of any investigations, inquiries, actions or other proceedings pending before or threatened by any Regulatory Authority or other Governmental Authority in the Territory with respect to the Licensed Products in the Field in the Territory arising from any default by Tetraphase or any of its Affiliates or a Third Party acting on behalf Tetraphase in the discovery, Research or Development of the Licensed Products;

(i) to Tetraphase's knowledge, the Existing Patents represent all Patent Rights that Tetraphase or its Affiliates own, Control or, to Tetraphase's knowledge, otherwise have rights under, as of the Effective Date that Cover the Development or Commercialization of the Licensed Product in the Field in the Territory in accordance with this Agreement. To Tetraphase's knowledge, there is no Know-How owned by or otherwise in the possession or control of Tetraphase or any of its Affiliates as of the Effective Date that is necessary or reasonably useful for the Development or Commercialization of the Licensed Product in the Field in the Territory that is not within the Tetraphase Know-How;

(j) except with respect to the rights granted to or retained by Harvard or any Governmental Authority under the Harvard Agreement, neither Tetraphase nor any of its Affiliates has licensed or otherwise encumbered its right, title or interest under the Existing Patents, Tetraphase Know-How or Existing Regulatory Documents (including by granting any covenant not to sue with respect thereto) in a manner that is inconsistent with the rights and licenses granted to Licensee under this Agreement;

(k) Tetraphase has obtained from its Affiliates the licenses and other rights necessary for Tetraphase to grant to Licensee the rights and licenses provided herein and for Licensee to perform its obligations hereunder;

(l) to Tetraphase's knowledge, each of the Existing Patents properly identifies each and every inventor of the claims thereof as determined in accordance with the Laws of the jurisdiction in which such Existing Patent is issued or pending;

(m) Tetraphase owns or otherwise Controls the Existing Patents, and owns or otherwise Controls any Tetraphase Know-How existing as of the Effective Date;

(n) to Tetraphase's knowledge, Tetraphase and its Affiliates have generated, prepared, maintained and retained all Regulatory Documents that is required to be maintained or retained pursuant to and in accordance with, as applicable, GLP and GCP and applicable Law; and

(o) to Tetraphase's knowledge, true, complete and correct copies (as of the Effective Date) of all material adverse information with respect to the safety and efficacy of the Licensed Products known to Tetraphase have been provided to Licensee prior to the Effective Date.

**Section 11.04** **Additional Licensee Warranties and Covenants.** Licensee hereby represents, warrants and covenants to Tetraphase that:

(a) Licensee has the capability to Develop, obtain Regulatory Approval and, if applicable, Reimbursement Approval for, and Commercialize Licensed Products as contemplated in this Agreement; and

(b) each Licensee Entity (other than Licensee) and each Licensee Entity's employees and permitted agents and contractors have executed agreements or have existing obligations under applicable Laws, or, upon their engagement by Licensee or any of its Affiliates, will execute such agreements, requiring automatic assignment to Licensee of all Inventions or other Know-how identified, discovered, authored, developed, conceived or reduced to practice during the course of and as the result of their association with Licensee or its Affiliates, and all intellectual property rights therein, and obligating the relevant individual or entity to maintain as confidential Licensee's confidential information related to any Licensed Product, Eravacycline Product or Eravacycline Materials as well as confidential information of other parties (including Tetraphase and its Affiliates) which such individual or entity may receive, to the extent required to support Licensee's obligations under this Agreement.

**Section 11.05** **Additional Tetraphase Warranty and Covenant**. Tetraphase hereby represents and warrants to Licensee as of the Effective Date that (a) it has provided a true, complete and correct copy of each In-License Agreement listed on Exhibit E, as amended, and (b) to Tetraphase's knowledge, Tetraphase is not, and has not been, in material breach of any In-License Agreement listed on Exhibit E. Tetraphase (a) will use commercially reasonable efforts to comply with each In-License Agreement to the extent such obligations have not been delegated to Licensee and to the extent that failure to do so would materially adversely affect Licensee's rights hereunder and (b) will not, without Licensee's prior written consent, amend or otherwise modify or permit to be amended or modified, any In-License Agreement in a manner that would materially adversely affect the rights and licenses granted to Licensee under this Agreement.

**Section 11.06** **Anti-Corruption.**

(a) Anti-Corruption Provisions. Each Party represents and warrants to the other Party that such Party has not, directly or indirectly, offered, promised, paid, authorized or given, and each Party agrees that such Party will not, in the future, offer, promise, pay, authorize or give, money or anything of value, directly or indirectly, to any Government Official (as defined below) or Other Covered Party (as defined below) for the purpose, pertaining to this Agreement, of: (i) influencing any act or decision of such Government Official or Other Covered Party; (ii) inducing such Government Official or Other Covered Party to do or omit to do an act in violation of a lawful duty; (iii) securing any improper advantage; or (iv) inducing such Government Official or Other Covered Party to influence the act or decision of a Governmental Authority, in order to obtain or retain business, or direct business to, any person or entity, in any way related to this Agreement.

For purposes of this Agreement: (A) "**Government Official**" means any official, officer, employee or representative of: (1) any Governmental Authority; (2) any public international organization or any department or agency thereof; or (3) any company or other entity owned or controlled by any Governmental Authority; and (B) "**Other Covered Party**" means any political party or party official, or any candidate for political office.

(b) Anti-Corruption Compliance.

(i) In performing under this Agreement, each Party, on behalf of itself and its respective Affiliates, agrees to comply with all applicable anti-corruption Laws, including the Foreign Corrupt Practices Act of 1977, as amended from time to time ("**FCPA**") and all anti-corruption Laws of the Territory.

(ii) Each Party represents and warrants to the other Party that such Party is not aware of any Government Official or Other Covered Party having any financial interest in the subject matter of this Agreement or in any way personally benefiting, directly or indirectly, from this Agreement.

(iii) No Party, nor any Affiliate of any Party, shall give, offer, promise or pay any political contribution or charitable donation at the request of any Government Official or Other Covered Party that is in any way related to this Agreement or any related activity.

(iv) In the event that a Party violates the FCPA, any anti-corruption Law of the Territory or any other applicable anti-corruption Law, or breaches any provision in this **Section 11.06 (Anti-Corruption)**, the other Party shall have the right to unilaterally terminate this Agreement pursuant to **Section 14.03** (**Termination for Breach**), subject to the cure periods therein.

**Section 11.07 Disclaimer**. EXCEPT AS EXPRESSLY SET FORTH HEREIN, THE INTELLECTUAL PROPERTY RIGHTS PROVIDED BY TETRAPHASE TO LICENSEE HEREIN ARE PROVIDED "AS IS" AND WITHOUT WARRANTY. EXCEPT AS EXPRESSLY SET FORTH HEREIN, EACH OF THE PARTIES EXPRESSLY DISCLAIMS ANY AND ALL WARRANTIES OF ANY KIND, EXPRESS OR IMPLIED, INCLUDING THE WARRANTIES OF DESIGN, MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE, VALIDITY OR ENFORCEABILITY OF THEIR RESPECTIVE INTELLECTUAL PROPERTY RIGHTS, AND NONINFRINGEMENT OF THE INTELLECTUAL PROPERTY RIGHTS OF THIRD PARTIES.

**Section 11.08 Limitation of Liability**. NEITHER PARTY SHALL BE ENTITLED TO RECOVER FROM THE OTHER PARTY ANY SPECIAL, INCIDENTAL, EXEMPLARY, INDIRECT, CONSEQUENTIAL OR PUNITIVE DAMAGES OR DAMAGES FOR LOSS OF PROFIT OR LOST OPPORTUNITY IN CONNECTION WITH THIS AGREEMENT, ITS PERFORMANCE OR LACK OF PERFORMANCE HEREUNDER, OR ANY LICENSE GRANTED HEREUNDER. THE FOREGOING SHALL NOT LIMIT (a) ANY INDEMNIFICATION OBLIGATIONS HEREUNDER OR (b) REMEDIES AVAILABLE TO EITHER PARTY WITH RESPECT TO A BREACH OF **ARTICLE XII** (**CONFIDENTIALITY)** OR **SECTION 2.06** OR FRAUD COMMITTED BY THE OTHER PARTY.

## ARTICLE XII.

## CONFIDENTIALITY

**Section 12.01** **Generally**. During the Term and for a period of [**] years thereafter, each Party (a) shall maintain in confidence all Confidential Information of the other Party; (b) shall not use such Confidential Information for any purpose except to fulfill its obligations or exercise its rights under this Agreement; and (c) shall not disclose such Confidential Information to anyone other than those of its Affiliates, directors, investors, prospective investors, lenders, prospective lenders, acquirers, prospective acquirers, licensees, prospective licensees, sublicensees, prospective sublicensees, employees, consultants, financial or legal advisors, or other agents or contractors (collectively, "**Representatives**") who are bound by written obligations of nondisclosure and non-use no less stringent than those set forth in this **ARTICLE XII (Confidentiality)** and to whom such disclosure, under this Agreement or the Confidentiality Agreement, is necessary in connection with the fulfillment of such Party's obligations or exercise of such Party's rights under this Agreement or in connection with *bona fide* financing or acquisition activities. Each Party shall (y) ensure that such Party's Representatives who receive any of the other Party's Confidential Information comply with the obligations set forth in this **ARTICLE XII (Confidentiality)** and (z) be responsible for any breach of these obligations by any of its Representatives who receive any of the other Party's Confidential Information. Each Party shall notify the other Party promptly on discovery of any unauthorized use or disclosure of the other's Confidential Information. Notwithstanding anything to the contrary in this **ARTICLE XII** (**Confidentiality**), Tetraphase may disclose Licensee's Confidential Information to each Third Party counterparty under any In-License Agreement as reasonably required to fulfill Tetraphase's obligations under such In-License Agreement, and Licensee acknowledges and agrees that, with respect to any such Confidential Information, such Third Party counterparty(ies) shall only be bound by the confidentiality obligations set forth in the applicable In-License Agreement(s).

**Section 12.02** **Exceptions**. The obligations of confidentiality, non-disclosure, and non-use set forth in **Section 12.01 (Generally)** shall not apply to, and "Confidential Information" shall exclude, any information to the extent the receiving Party (the "**Recipient**") can demonstrate that such information: (a) was in the public domain or publicly available at the time of disclosure to the Recipient or any of its Affiliates by the disclosing Party or any of its Affiliates pursuant to this Agreement or the Confidentiality Agreement, or thereafter entered the public domain or became publicly available, in each case other than as a result of any action of the Recipient, or any of its Representatives, in breach of this Agreement or the Confidentiality Agreement; (b) was rightfully known by the Recipient or any of its Affiliates (as shown by its written records) prior to the date of disclosure to the Recipient or any of its Affiliates by the disclosing Party or any of its Affiliates pursuant to this Agreement or the Confidentiality Agreement; (c) was received by the Recipient or any of its Affiliates on an unrestricted basis from a Third Party rightfully in possession of such information and not under a duty of confidentiality to the disclosing Party or any of its Affiliates; or (d) was independently developed by or for the Recipient or any of its Affiliates without reference to or reliance on the Confidential Information of the other Party or any of its Affiliates (as demonstrated by written records).

**Section 12.03** **Permitted Disclosures**. Notwithstanding any other provision of this Agreement, Recipient's (or its Affiliates') disclosure of the other Party's Confidential Information shall not be prohibited if such disclosure: (a) is in response to a valid order of a court or other Governmental Authority; or (b) is otherwise required by applicable Law or rules of a nationally recognized securities exchange or NASDAQ. If a Recipient is required to disclose Confidential Information pursuant to **Section 12.03(a)** or **Section 12.03(b)**, prior to any disclosure the Recipient shall, to the extent practicable, provide the disclosing Party with prior written notice of such disclosure in order to permit the disclosing Party to seek a protective order or other confidential treatment of such disclosing Party's Confidential Information. Further, notwithstanding any other provision of this Agreement but subject to (i) **Section 12.01 (Generally)** with respect to disclosures to Representatives and (ii) if applicable, the first two sentences of this **Section 12.03 (Permitted Disclosures)**, either Party may disclose the other Party's Confidential Information to the extent necessary to fulfill the obligations imposed on the Recipient under this Agreement or exercise the rights granted to or retained by the Recipient under this Agreement, including in filing or prosecuting patent applications, prosecuting or defending litigation, responding to an investigation by a Governmental Authority, or otherwise establishing rights or fulfilling or enforcing obligations under this Agreement, making Regulatory Filings with respect to any Licensed Product in the Field in the Territory (if the Recipient is Licensee) or any Eravacycline Product outside of the Territory (if the Recipient is Tetraphase), or conducting Development, or Commercialization with respect to any Licensed Product in the Field in the Territory (if the Recipient is Licensee) or conducting Development or Commercialization with respect to the Licensed Compound or any Eravacycline Product outside the Territory or Researching or Manufacturing the Licensed Compound or any Eravacycline Product (if the Recipient is Tetraphase).

**Section 12.04** **Publicity**. The Parties recognize that each Party may from time to time desire to issue press releases and make other public statements or public disclosures regarding the terms of this Agreement. In such event, the Party desiring to issue a press release or make a public statement or public disclosure shall provide the other Party with a copy of the proposed press release, statement or disclosure for review and approval as soon as practicable prior to publication, which advance approval shall not be unreasonably withheld, conditioned or delayed. No other public statement or public disclosure of, or concerning, the terms of this Agreement shall be made, either directly or indirectly, by either Party, without first obtaining the written approval of the other Party. Once any public statement or public disclosure has been approved in accordance with this **Section 12.04** (**Publicity**), then either Party may appropriately communicate information contained in such permitted statement or disclosure. Notwithstanding anything to the contrary in this **ARTICLE XII** (**Confidentiality**), (a) a Party may disclose the terms of this Agreement where required, as reasonably determined by the disclosing Party, by applicable Law or legal process or by applicable stock exchange or NASDAQ rule (with prompt notice of any such legally required disclosure to the other Party and to the extent practicable an opportunity to comment on such disclosure), (b) a Party may disclose the terms of this Agreement under obligations of confidentiality and non-use that are at least as stringent as those set forth in **ARTICLE XII** (**Confidentiality**) to such Party's Representatives in connection with such Party's fulfillment of obligations or exercise of rights hereunder or in connection with such Party's *bona fide* financing or acquisition activities, and (c) Tetraphase may disclose the terms of this Agreement to any Third Party counterparty under any In-License Agreement, and Licensee acknowledges and agrees that, with respect to the terms of

this Agreement, each such Third Party counterparty shall only be bound by the confidentiality obligations set forth in the applicable In-License Agreement(s).

**Section 12.05** **Publications**. Tetraphase acknowledges Licensee's interest in publishing certain key results of Licensee's Development and Commercialization of Licensed Products in the Field in the Territory. Licensee recognizes the mutual interest in obtaining valid patent protection and Tetraphase's interest in protecting its trade secret information. Consequently, except for disclosures permitted pursuant to **Section 12.02 (Exceptions)**, **Section 12.03 (Permitted Disclosures)** or **Section 12.04 (Publicity)**, if Licensee wishes to make a publication or public presentation with respect to the Development, Manufacturing or Commercialization of Licensed Products in the Field in the Territory, Licensee shall deliver to Tetraphase a copy of the proposed written publication or presentation within [**] days prior to submission for publication or presentation. Tetraphase shall have the right (a) to require modifications to the publication or presentation for patentability reasons or trade secret reasons, and Licensee will remove all of Tetraphase's Confidential Information if requested by Tetraphase and (b) to require a reasonable delay in publication or presentation in order to protect patentable information. If Tetraphase requests a delay, then Licensee shall delay submission or presentation for a period of [**] days (or such shorter period as may be mutually agreed by the Parties) to enable Tetraphase to file patent applications protecting Tetraphase's rights in such information.

**Section 12.06** **Injunctive Relief**. Each Party acknowledges and agrees that there may be no adequate remedy at law for any breach of its obligations under this **ARTICLE XII (Confidentiality)**, that any such breach may result in irreparable harm to the other Party and, therefore, that upon any such breach or any threat thereof, such other Party may seek appropriate equitable relief in addition to whatever remedies it might have at law, without the necessity of showing actual damages.

## ARTICLE XIII.

## INDEMNIFICATION

**Section 13.01** **Indemnification by Tetraphase**. Tetraphase shall indemnify, hold harmless and defend Licensee and its Affiliates, and their respective directors, officers, consultants and employees (the "**Licensee Indemnitees**") from and against any and all Third Party suits, claims, actions, demands, liabilities, expenses, costs, damages, deficiencies, obligations or losses (including reasonable attorneys' fees, court costs, witness fees, damages, judgments, fines and amounts paid in settlement) ("**Losses**") to the extent that such Losses arise out of (a) any breach of this Agreement by Tetraphase, (b) the Development, Manufacture or Commercialization of the Licensed Compound or any Licensed Product by or on behalf of any Tetraphase Entity or (c) the gross negligence or willful misconduct of any Tetraphase Indemnitee. Notwithstanding the foregoing, Tetraphase shall not have any obligation to indemnify the Licensee Indemnitees to the extent that the applicable Losses arise out of the negligence or willful misconduct of any Licensee Indemnitee or any breach of this Agreement by Licensee.

**Section 13.02** **Indemnification by Licensee**. Licensee shall indemnify, hold harmless and defend Tetraphase and its Affiliates, and their respective directors, officers, employees and consultants (the "**Tetraphase Indemnitees**") from and against any and all Losses, to the extent that such Losses arise out of (a) any breach of this Agreement by Licensee, or any act or failure to act by any Licensee Entity that causes a breach of any In-License Agreement, (b) the Development or Commercialization of the Licensed Compound or any Licensed Product by or on behalf of any Licensee Entity or (c) the gross negligence or willful misconduct of any Licensee Indemnitee. Notwithstanding the foregoing, Licensee shall not have any obligation to indemnify the Tetraphase Indemnitees to the extent that the applicable Losses arise out of the negligence or willful misconduct of any Tetraphase Indemnitee or any breach of this Agreement by Tetraphase.

**Section 13.03** **Procedure**. In the event of a claim by a Third Party against an Licensee Indemnitee or Tetraphase Indemnitee entitled to indemnification under this Agreement ("**Indemnified Party**"), the Indemnified Party shall promptly notify the Party obligated to provide such indemnification ("**Indemnifying Party**") in writing of the claim and the Indemnifying Party shall undertake and solely manage and control, at its sole expense, the defense of the claim and its settlement. The Indemnified Party shall cooperate with the Indemnifying Party. The Indemnified Party may, at its option and expense, be represented in any such action or proceeding by counsel of its choice. The Indemnifying Party shall not be liable for any litigation costs or expenses incurred by the Indemnified Party without the Indemnifying Party's written consent. The Indemnifying Party shall not settle any such claim unless such settlement fully and unconditionally releases the Indemnified Party from all liability relating thereto and does not impose any obligations on the Indemnified Party, unless the Indemnified Party otherwise agrees in writing. No Indemnified Party may settle any claim for which it is being indemnified under this Agreement without the Indemnifying Party's prior written consent.

**Section 13.04** **Insurance**. Licensee shall, at its own expense, obtain and maintain insurance with a reputable insurance carrier with respect to the Licensee Entities' Development and Commercialization of Licensed Products in the Field in the Territory under this Agreement in such type and amount and subject to such deductibles and other limitations as biopharmaceutical companies in the Territory customarily maintain with respect to the Development and Commercialization of similar products, but in any event no less than [**] Dollars ($[**]) per incident and [**] Dollars ($[**]) annual aggregate. Such insurance policy shall provide product liability coverage and broad form contractual liability coverage for Licensee's indemnification obligations under this Agreement and shall name the Tetraphase Indemnitees and the Harvard Indemnitees as additional insureds. Licensee shall provide a copy of such insurance policy to Tetraphase upon reasonable request by Tetraphase (and, by way of example and not limitation, any request by Tetraphase made [**], or at Harvard's request, shall be considered reasonable). Licensee shall provide Tetraphase with written notice at least [**] days prior to any cancellation, non-renewal or material change in such insurance. If Licensee does not obtain replacement insurance providing comparable coverage within such [**] day period, Tetraphase shall have the right to terminate this Agreement effective at the end of such [**] day period without notice or any additional waiting periods. This **Section 13.04 (Insurance)** shall survive expiration or termination of this Agreement and last until [**] years after the last sale of any Licensed Product in the Field in the Territory (or Terminated Territory, as applicable) by any Licensee Entity.

**Section 13.05** **Indemnification of Harvard**. Licensee shall indemnify, hold harmless and defend Harvard and its current or former directors, governing board members, trustees, officers, faculty, medical and professional staff, employees, students and agents and their respective successors, heirs and assigns (collectively, the "**Harvard Indemnitees**") from and against any and all Losses, to the extent that such Losses arise out of, are based upon, or otherwise relate to (a) any acts or omissions of Licensee, its Affiliates or any of its sublicensees in connection with Licensed Products or this Agreement or (b) product liability concerning any product, process, or service made, used or sold pursuant to any right or license granted under this Agreement. Licensee shall not settle any claim for which a Harvard Indemnitee seeks indemnification from Licensee unless such settlement fully and unconditionally releases Harvard from all liability relating thereto, does not impose any obligations on the Harvard Indemnitee and does not limit the scope, validity or enforceability of any Licensed Patent Right (as defined in the Harvard Agreement), unless Harvard otherwise agrees in writing. Licensee shall, at its own expense, provide attorneys reasonably acceptable to Harvard to defend against any such claim, whether or not such actions are rightfully brought.

## ARTICLE XIV.

## TERM AND TERMINATION

**Section 14.01** **Term**. The term of this Agreement shall begin on the Effective Date and, unless earlier terminated in accordance with the terms of this **ARTICLE XIV** (**Term and Termination**), will expire upon the later of (a) expiration of the last-to-expire Royalty Term or (b) the expiration of the Harvard Agreement (the "**Term**").

**Section 14.02** **Termination for Patent Right Challenge.** In the event that any Licensee Entity challenges, or assists any individual or entity in challenging, the validity, patentability or enforceability of any Patent Right that (a) is owned by or licensed to Tetraphase or any of its Affiliates and (b) Covers or otherwise claims the Licensed Compound or any Eravacycline Product or their respective Research, Development, Manufacture or Commercialization anywhere in the world, or otherwise opposes the validity, patentability or enforceability of any such Patent Right (except, in each case, as required by Law), then, to the extent consistent with applicable Law, Tetraphase may immediately terminate this Agreement by providing written notice thereof to Licensee.

**Section 14.03** **Termination for Breach**. Subject to the terms and conditions of this **Section 14.03** (**Termination for Breach**), a Party (the "**Non-Breaching Party**") shall have the right, in addition to any other rights and remedies available to such Party at law or in equity, to terminate this Agreement in the event the other Party (the "**Breaching Party**") is in material breach of its obligations under this Agreement. The Non-Breaching Party shall first provide written notice to the Breaching Party, which notice shall identify with particularity the alleged breach (the "**Breach Notice**"). With respect to material breaches of any payment provision hereunder, the Breaching Party shall have a period of [**] days after such Breach Notice is provided to cure such breach. With respect to all other breaches, the Breaching Party shall have a period of [**] days after such Breach Notice is provided to cure such breach. Notwithstanding anything to the contrary in this **Section 14.03** (**Termination for Breach**), with respect to any breach by Licensee that results, or could reasonably be expected to result in, a

breach of any In-License Agreement, Licensee shall have a period of [**] days after Tetraphase provides written notice to Licensee that Tetraphase has received a written notice of breach from the applicable Third Party licensor to cure such breach. If such breach is not cured within the applicable period set forth above, the Non-Breaching Party may, at its election, terminate this Agreement upon written notice to the Breaching Party; *provided* that, if a material breach pertains only to facts relating to one or more Jurisdictions other than mainland China, then the Non-Breaching Party shall only have the right to terminate this Agreement only with respect to such Jurisdiction(s); *provided*, further, that, solely with respect to any breach (other than a breach of any payment provision) that is not reasonably likely to result in a breach of any In-License Agreement, the termination shall not become effective for [**] days after the Breach Notice if the breach specified in such Breach Notice cannot be cured within the initial [**] day cure period, and if the Breaching Party commenced actions to cure such breach within the initial [**] day cure period and thereafter diligently continued such actions and cured such breach within such [**] day period. The waiver by either Party of any breach of any term or condition of this Agreement shall not be deemed a waiver as to any subsequent or similar breach. In the event Licensee is entitled to terminate this Agreement in its entirety pursuant to this **Section 14.03 (Termination for Breach)**, as an alternative to such termination, Licensee may elect upon written notice to Tetraphase that, as an alternative to such termination, from the date on which such termination would otherwise have become effective, any royalties otherwise payable by Licensee to Tetraphase pursuant to **Section 8.04 (Royalties)** shall be reduced by [**] percent ([**]%) and, for clarity, this Agreement shall otherwise continue in full force and effect. Such election by Licensee of a royalty reduction as an alternative to termination for a breach shall not be deemed a waiver as to any subsequent or similar breach.

**Section 14.04** [Intentionally Left Blank].

**Section 14.05** **Termination for Bankruptcy and Rights in Bankruptcy.**

(a) To the extent permitted under applicable Law, if, at any time during the Term, an Event of Bankruptcy (as defined below) relating to either Party (the "**Bankrupt Party**") occurs, the other Party (the "**Other Party**") shall have, in addition to all other legal and equitable rights and remedies available to such Party, the option to terminate this Agreement upon sixty (60) days written notice to the Bankrupt Party. It is agreed and understood that, if the Other Party does not elect to terminate this Agreement upon the occurrence of an Event of Bankruptcy, except as may otherwise be agreed with the trustee or receiver appointed to manage the affairs of the Bankrupt Party, the Other Party shall continue to make all payments required of it under this Agreement as if the Event of Bankruptcy had not occurred, and the Bankrupt Party shall not have the right to terminate any license granted herein. The term "**Event of Bankruptcy**" means: (a) filing in any court or agency pursuant to any statute or regulation of any state or country, a petition in bankruptcy or insolvency or for reorganization or for an arrangement or for the appointment of a receiver or trustee of the Bankrupt Party or of its assets or (b) being served with an involuntary petition against the Bankrupt Party, filed in any insolvency proceeding, where such petition is not dismissed within sixty (60) days after the filing thereof.

(b) All rights and licenses granted under or pursuant to this Agreement by Licensee and Tetraphase are and shall otherwise be deemed to be, for purposes of Section 365(n) of the

U.S. Bankruptcy Code or any analogous provisions in any other country or jurisdiction, licenses of right to "intellectual property" as defined under Section 101 of the U.S. Bankruptcy Code. The Parties agree that the Parties, as licensees of such rights under this Agreement, shall retain and may fully exercise all of their rights and elections under the U.S. Bankruptcy Code or any analogous provisions in any other country or jurisdiction. The Parties further agree that, in the event of the commencement of a bankruptcy proceeding by or against either Party under the U.S. Bankruptcy Code or any analogous provisions in any other country or jurisdiction, the Party hereto that is not a Party to such proceeding shall be entitled to a complete duplicate of (or complete access to, as appropriate) any such intellectual property and all embodiments of such intellectual property, which, if not already in the non-subject Party's possession, shall be promptly delivered to it (i) upon any such commencement of a bankruptcy proceeding upon the non-subject Party's written request therefor, unless the Party subject to such proceeding elects to continue to perform all of its obligations under this Agreement or (ii) if not delivered under clause (i) above, following the rejection of this Agreement by or on behalf of the Party subject to such proceeding upon written request therefor by the non-subject Party. The Parties acknowledge and agree that payments made under **Section 8.02 (Development Milestone Payments)** or **Section 8.03 (Sales Milestone Payments)** or pursuant to any Supply Agreements shall not (x) constitute royalties within the meaning of Section 365(n) of the U.S. Bankruptcy Code or any analogous provisions in any other country or jurisdiction or (y) relate to licenses of intellectual property hereunder.

**Section 14.06** **Automatic Termination of In-Licensed Rights**. Upon any termination of the Harvard License in whole or in part, any Patent Rights or other intellectual property rights that, pursuant to such termination, Tetraphase has ceased to Control shall be excluded from the Patent Rights and intellectual property licensed to Licensee pursuant to **Section 2.01 (Grant of Rights)**. Upon such termination due to any act or failure to act by any Licensee Entity, then Licensee shall use commercially reasonable efforts, only to the extent requested by Tetraphase in writing and only to the extent permitted pursuant to the Harvard Agreement, (A) negotiate a direct license from Harvard pursuant to Section 4.2.2.3 of the Harvard Agreement that permits Licensee to sublicense the rights granted under such direct license to Tetraphase (and, to the extent possible, Licensee shall ensure that such direct license contains terms no less favorable to Licensee than the terms of the Harvard Agreement are to Tetraphase as of the Effective Date) and (B) exclusively sublicense such rights to Tetraphase on terms no less favorable than those in Licensee's direct license agreement with Harvard. Upon any other such termination (i.e., other than due to any act or failure to act by any Licensee Entity), then Licensee shall, at its sole discretion, have the right to negotiate a direct license from Harvard to the extent set forth in Section 4.2.2.3 of the Harvard Agreement.

**Section 14.07** **Effect of Termination**.

(a) In the event of any termination of this Agreement in its entirety, the following shall apply:

(i) All license grants in this agreement from Tetraphase to Licensee shall immediately terminate;

(ii) To the extent permitted under applicable Law, Licensee shall promptly wind down all clinical trials then being conducted with respect to any Licensed Product in the Territory; *provided* that Licensee shall be permitted to take all reasonable steps necessary to minimize liability and harm to patients in this process;

(iii) Licensee shall cease using the Tetraphase Technology and return all inventory of the Eravacycline Materials to Tetraphase, together with all copies of the Tetraphase Know-How and other Confidential Information of Tetraphase in the possession or control of Licensee or any of its Representatives;

(iv) Licensee shall, at Tetraphase's written request, to the extent feasible under applicable Law, promptly: (A) assign and transfer to Tetraphase all of the Licensee Entities' right, title, and interest in and to all Licensee Regulatory Documents (including Regulatory Approvals), clinical trial agreements (to the extent assignable and not cancelled), confidentiality and other agreements, and materials and Know-How relating exclusively to clinical trials of any Licensed Product, in each case solely to the extent related to and necessary or useful for the Research, Development, Manufacture or Commercialization of the Licensed Compound or any Licensed Product, and solely to the extent in Licensee's possession or control, and Licensee Trademarks (including all goodwill associated therewith and each Internet domain name incorporating any Licensee Trademark or any variation or part of any Licensee Trademark as its URL address or any part of such address) relating to the Research, Development, Manufacture or Commercialization of the Licensed Compound or any Eravacycline Product and (B) disclose to Tetraphase all documents embodying the foregoing that are in any Licensee Entity's possession or control or that any Licensee Entity is able to obtain using reasonable efforts;

(v) The costs associated with the activities set forth in subsections (a)(ii), (a)(iii), (a)(iv)(A) and (a)(iv)(B) of this **Section 14.07 (Effect of Termination)** shall be borne by Licensee; and

(vi) Notwithstanding any expiration or termination of this Agreement, the Safety Data Exchange Agreement (with respect to Licensee's obligations thereunder) shall continue in accordance with its terms.

(b) In the event of any termination in respect of one or more Jurisdictions (such Jurisdictions (or, in the event that this Agreement is terminated in its entirety, all Jurisdictions), the "**Terminated Territory**") (but not in the case of any termination of this Agreement in its entirety), the following shall apply:

(i) All rights and licenses granted by Tetraphase to Licensee, shall automatically be deemed to be amended to exclude the Terminated Territory;

(ii) To the extent permitted under applicable Law, Licensee shall promptly wind down all clinical trials then being conducted with respect to any Licensed Product in the Terminated Territory; *provided* that Licensee shall be permitted to take all reasonable steps necessary to minimize liability and harm to patients in this process;

(iii) All Licensee diligence obligations with respect to the Terminated Territory shall terminate;

(iv) Licensee shall, at Tetraphase's written request, to the extent feasible under applicable Law, promptly: (A) assign and transfer to Tetraphase all of the Licensee Entities' right, title, and interest in and to all Licensee Regulatory Documents (including Regulatory Approvals), clinical trial agreements (to the extent assignable and not cancelled), confidentiality and other agreements, and materials and Know-How relating exclusively to clinical trials of any Licensed Product in the Terminated Territory, in each case solely to the extent exclusively related to Licensed Product the Terminated Territory, and solely to the extent in Licensee's possession or control, and Licensee Trademarks in the Terminated Territory (including all goodwill associated therewith and each Internet domain name incorporating any Licensee Trademark or any variation or part of any Licensee Trademark as its URL address or any part of such address) and (B) disclose to Tetraphase all documents embodying the foregoing that are in any Licensee Entity's possession or control or that any Licensee Entity is able to obtain using reasonable efforts; and

(v) The costs associated with the activities set forth in subsections (b)(ii), (b)(iv)(A) and (b)(iv)(B) of this **Section 14.07 (Effect of Termination)** shall be borne by Licensee.

**Section 14.08** **Survival; Accrued Rights**. The following articles and sections of this Agreement shall survive expiration or early termination for any reason: **ARTICLE I** (**Definitions**), **Section 2.01(c)**, **Section 2.01(d)**, **Section 2.01(e)**, **Section 2.03 (No Other Rights and Retained Rights)**, **Section 2.04(c)(ii)**, **Section 2.05 (In-License Agreements)** (solely to the extent applicable to Licensee's exercise of any rights, or performance of any obligations, retained by Licensee hereunder following the applicable expiration or termination), **Section 2.06 (Exclusivity)**, **Section 6.06(a)**, **ARTICLE VIII** (**Payments**) (solely with respect to any payment obligations incurred prior to expiration or termination), **Section 9.01** (**Tetraphase Intellectual Property**), **Section 9.02** (**Licensee Intellectual Property**), **Section 9.03** (**Joint Technology**), **Section 9.04 (Prosecution of Patent Rights)** (with respect to Joint Patent Rights), **Section 9.05 (Enforcement and Defense)** (with respect to Joint Patent Rights), **Section 9.06 (Defense of Third Party Infringement and Misappropriation Claims)** (with respect to Third Party claims regarding infringement or misappropriation during the Term), **Section 11.07 (Disclaimer)**, **Section 11.08 (Limitation of Liability)**, **ARTICLE XII** (**Confidentiality**), **ARTICLE XIII** (**Indemnification**), **Section 14.06 (Automatic Termination of In-Licensed Rights)** (second and third sentences only), **Section 14.07** (**Effect of Termination**), **Section 14.08** (**Survival; Accrued Rights**), **ARTICLE XV** (**Dispute Resolution; Governing Law**), and **ARTICLE XVI** (**Miscellaneous**). In any event, expiration or termination of this Agreement shall not relieve either Party of any liability which accrued hereunder prior to the effective date of such

expiration or termination nor preclude either Party from pursuing all rights and remedies it may have hereunder or at law or in equity with respect to any breach of this Agreement, nor prejudice either Party's right to obtain performance of any obligation.

## ARTICLE XV.

## DISPUTE RESOLUTION; GOVERNING LAW

**Section 15.01** **Arbitration**. Subject to **Section 15.01(d) (Intellectual Property Disputes)**, any disputes, claims or controversies in connection with this Agreement, including any questions regarding its formation, existence, validity, enforceability, performance, interpretation, breach or termination, that are not resolved in accordance with **ARTICLE III (Governance)** shall be referred to and finally resolved by binding arbitration under the International Chamber of Commerce Rules of Arbitration (the "**Rules**"), which rules are deemed to be incorporated by reference into this **Section 15.01** (**Arbitration**), in the manner described below:

(a) Arbitration Request. If a Party intends to begin an arbitration to resolve a dispute arising under this Agreement, such Party shall provide written notice (the "**Arbitration Request**") to the other Party of such intention and the issues for resolution.

(b) Additional Issues. Within [**] days after the receipt of an Arbitration Request, the other Party may, by written notice, add additional issues for resolution.

(c) Arbitration Procedure. The seat of arbitration will be in Singapore unless other venue is agreed upon by Parties, and it will be conducted in the English language. The arbitrators may not decide based on equity. Unless agreed by the Parties to choose a single common arbitrator, the arbitration will be conducted by three arbitrators, one appointed by each Party, according to the Rules. The two arbitrators appointed by the Parties will by mutual agreement appoint the third arbitrator, who will preside over the arbitration. Any dispute or omission regarding the appointment of the arbitrators by the Parties, as well as the choice of the third arbitrator, will be resolved by the International Chamber of Commerce ("**ICC**"). The arbitral award shall be final, definitive and binding on the Parties and their successors. The Parties reserve the right to apply to a competent judicial court to obtain urgent remedies to protect rights before establishment of the arbitration panel, without such recourse being considered as a waiver of arbitration. Except as otherwise determined by the arbitrators, the Parties shall each bear half of the fees and expenses of the arbitrators and the ICC, and each Party shall bear the costs and fees of its attorneys. Nothing in this Agreement shall be deemed as preventing either Party from seeking injunctive relief (or any other provisional remedy) from any court having jurisdiction over the Parties and the subject matter of the dispute as necessary to protect either Party's name, Confidential Information, Know-How, intellectual property rights or any other proprietary right or otherwise to avoid irreparable harm. If the issues in dispute involve scientific or technical matters, any arbitrator chosen hereunder shall have educational training or experience sufficient to demonstrate a reasonable level of knowledge in the field of biotechnology and pharmaceuticals. Judgment on the award rendered by the arbitrator may be entered in any court having jurisdiction thereof.

(d) Intellectual Property Disputes. Unless otherwise agreed by the Parties, a dispute between the Parties relating to the validity or enforceability of any Patent Right shall not be subject to arbitration and shall be submitted to a court or patent office of competent jurisdiction in the relevant country in which such patent was issued or, if not issued, in which the underlying patent application was filed. The Parties submit to the jurisdiction of such court or patent office and irrevocably waive any assertion that the case should be heard in a different venue or forum.

**Section 15.02** **Choice of Law**. This Agreement and all amendments, modifications, alterations, or supplements hereto, and the rights of the Parties hereunder, shall be construed under and governed by the Laws of the State of New York, exclusive of its conflicts of laws principles.

**Section 15.03** **Language**. This Agreement has been prepared in the English language and the English language shall control its interpretation. All consents, notices, reports and other written documents to be delivered or provided by a Party under this Agreement shall be in the English language, and in the event of any conflict between the provisions of any document and the English language translation thereof, the terms of the English language translation shall control.

## ARTICLE XVI.

## MISCELLANEOUS

**Section 16.01** **Assignment**.

(a) Tetraphase may assign this Agreement without the prior written consent of Licensee (i) to any Affiliate of Tetraphase, *provided* that Tetraphase remains fully liable for the performance of Tetraphase's obligations hereunder by such Affiliate and Tetraphase informs Licensee of such assignment or (ii) to a successor in connection with a merger or consolidation of Tetraphase or the sale of all or substantially all of that portion of Tetraphase's assets or Tetraphase's business to which this Agreement relates, in which case Tetraphase will provide prior written notice to Licensee.

(b) Licensee may not assign this Agreement without the prior written consent of Harvard and Tetraphase, except that Licensee may assign this Agreement to an Affiliate of Licensee or to a successor in connection with the merger, consolidation or sale of all or substantially all of Licensee's assets or that portion of Licensee's business to which this Agreement relates; *provided, however*, that any permitted assignee agrees in writing in a manner reasonably satisfactory to Harvard to be bound by the terms of this Agreement.

(c) Any assignment in violation of this **Section 16.01** (**Assignment**) shall be null and void. This Agreement shall be binding on and shall inure to the benefit of the permitted successors and assigns of the Parties.

**Section 16.02** **Acquisitions.** Each Party agrees that, in the event that a Party (the "**Acquired Party**") is acquired (whether by way of merger, acquisition, sale of all or substantially all of its business, or otherwise) or sells all or substantially all of its business or assets to which this Agreement pertains (an "**Acquisition**") by or to a Third Party (the

"**Acquirer**"), the non-Acquired Party shall not obtain any rights or access under this Agreement to any Know-How or Patent Rights owned by or licensed to such Acquirer, or any of such Acquirer's Affiliates that were not Affiliates of the Acquired Party immediately prior to the consummation of such Acquisition, that were not already within Tetraphase Technology (if the Acquired Party is Tetraphase) or Licensee Technology (if the Acquired Party is Licensee) immediately prior to the consummation of such Acquisition.

**Section 16.03** **Force Majeure**. Subject to the terms of each In-License Agreement, if either Party shall be delayed, interrupted in or prevented from the performance of any obligation hereunder by reason of force majeure, which may include any act of God, fire, flood, earthquake, war (declared or undeclared), public disaster, act of terrorism, government action, strike or labor differences, in each case outside of such Party's reasonable control, such Party shall not be liable to the other therefor, and the time for performance of such obligation shall be extended for a period equal to the duration of the force majeure which occasioned the delay, interruption or prevention. The Party invoking the force majeure rights of this **Section 16.03** (**Force Majeure**) must notify the other Party by courier or overnight dispatch (*e.g.*, Federal Express) within a period of thirty (30) days of both the first and last day of the force majeure unless the force majeure renders such notification impossible, in which case notification will be made as soon as possible. If the delay resulting from the force majeure exceeds one hundred eighty (180) days, the other Party may terminate this Agreement immediately upon written notice to the Party invoking the force majeure rights of this **Section 16.03** (**Force Majeure**).

**Section 16.04** **Entire Agreement**. This Agreement, together with the exhibits and schedules attached hereto, constitutes the entire agreement between Tetraphase or any of its Affiliates, on the one hand, and Licensee or any of its Affiliates, on the other hand, with respect to the subject matter hereof, supersedes all prior understandings and writings between Tetraphase or any of its Affiliates, on the one hand, and Licensee or any of its Affiliates, on the other hand relating to such subject matter, including the Confidentiality Agreement, and shall not be modified, amended or terminated, except by another agreement in writing executed by the Parties.

**Section 16.05** **Severability**. If, under applicable Law, any provision of this Agreement is invalid or unenforceable, or otherwise directly or indirectly affects the validity of any other material provision of this Agreement (such invalid or unenforceable provision, a "**Severed Clause**"), it is mutually agreed that this Agreement shall endure except for the Severed Clause. The Parties shall consult one another and use their reasonable efforts to agree upon a valid and enforceable provision that is a reasonable substitute for the Severed Clause in view of the intent of this Agreement.

**Section 16.06** **Notices**. Any notice or report required or permitted to be given under this Agreement shall be in writing and shall be mailed by internationally recognized express delivery service, or sent by facsimile and confirmed by mailing, as follows (or to such other address as the Party to whom notice is to be given may have furnished to the other Party in writing in accordance herewith):

If to Tetraphase:

Tetraphase Pharmaceuticals
480 Arsenal Way, Suite 110
Watertown, MA 02472
Attention: General Counsel
Facsimile: [**]

With a copy to (which shall not constitute notice for purposes of this Agreement):

WilmerHale
60 State Street
Boston, Massachusetts 02109
Attention: Belinda M. Juran
Facsimile: (617) 526-5000

If to Licensee:

Everest Medicines Limited
Suite 4508, 45F, Tower 2, Plaza 66
1266 Nanjing Xi Lu
Shanghai 200040
China
Attention: General Counsel
Fax: [**]

With a copy to (which shall not constitute notice for purposes of this Agreement):

Covington & Burling
2701 Two ifc, Shanghai ifc
No. 8 Century Avenue
Pudong New District
Shanghai 200120
Attention: Weishi Li
Facsimile: [**]

Any such notice shall be deemed to have been given (a) when delivered if personally delivered, (b) on receipt if sent by overnight courier or (c) on receipt if sent by mail.

**Section 16.07** **Agency**. Neither Party is, nor will be deemed to be a partner, employee, agent or representative of the other Party for any purpose. Each Party is an independent contractor of the other Party. Neither Party shall have the authority to speak for, represent or obligate the other Party in any way without prior written authority from the other Party.

**Section 16.08** **No Waiver**. Any omission or delay by either Party at any time to enforce any right or remedy reserved to it, or to require performance of any of the terms, covenants or provisions hereof, by the other Party, shall not constitute a waiver of such Party's rights to the future enforcement of any of its rights under this Agreement. Any waiver by a Party of a particular breach or default by the other Party shall not operate or be construed as a waiver of any subsequent breach or default by the other Party.

**Section 16.09** **Cumulative Remedies**. Except as may be expressly set forth herein, no remedy referred to in this Agreement is intended to be exclusive, but each shall be cumulative and in addition to any other remedy referred to in this Agreement or otherwise available under law or in equity.

**Section 16.10** **No Third Party Beneficiary Rights**. This Agreement is not intended to and shall not be construed to give any Third Party any interest or rights (including any third party beneficiary rights) with respect to or in connection with any agreement or provision contained herein or contemplated hereby, other than, (a) to the extent provided in **Section 13.01 (Indemnification by Tetraphase)**, the Licensee Indemnitees, (b) to the extent provided in **Section 13.02 (Indemnification by Licensee)**, the Tetraphase Indemnitees and (c) to the extent provided in **Section 13.05 (Indemnification of Harvard)**, and also with respect to **Section 13.04 (Insurance)**, the Harvard Indemnitees.

**Section 16.11** **Use of Harvard Name**. Licensee shall not, and shall ensure that its Affiliates and sublicensees shall not, use the name or insignia of Harvard or the name of any of Harvard's officers, faculty, other researchers or students, or any adaptation of such names, in any advertising, promotional or sales literature, including any press release or any document employed to obtain funds, without the prior written approval of Harvard. The restriction set forth in this **Section 16.11 (Use of Harvard Name)** shall not apply to any information required by Law to be disclosed to any Governmental Authority, including any information required to be disclosed pursuant to rules and regulations promulgated by the United States Securities and Exchange Commission or the rules and regulations of any stock exchange or NASDAQ.

**Section 16.12** **Performance by Affiliates, Sublicensees or Subcontractors**. To the extent that this Agreement imposes any obligation on any Affiliate, permitted sublicensee or permitted subcontractor of Licensee, Licensee shall cause such Affiliate, permitted sublicensee or permitted subcontractor (as applicable) to perform such obligation. Either Party may use one or more of its Affiliates to perform its obligations and duties hereunder; *provided* that such Party so notifies the other Party in writing and *provided*, *further*, that such Party shall remain liable hereunder for the prompt payment and performance of all of its obligations hereunder.

**Section 16.13** **Counterparts**. This Agreement may be executed in counterparts, all of which taken together shall be regarded as one and the same instrument.

*[Signature page follows]*

IN WITNESS WHEREOF, the Parties have executed this Agreement through their duly authorized representatives to be effective as of the Effective Date.

TETRAPHASE PHARMACEUTICALS, INC.

By: /s/ Guy Macdonald
Name: Guy Macdonald
Title: President and Chief Executive Officer

EVEREST MEDICINES LIMITED

By: /s/ Sean Wuxiong Cao
Name: Sean Wuxiong Cao
Title: President

**Exhibit A**

**List of Tetraphase Patent Rights Existing as of the Effective Date**

| Jurisdiction | Patent Application No. | Patent No. | Grant Date |
|---|---|---|---|
| [**] | | | |

**Exhibit B**

**Development Plan Framework**

*[see attached]*

Confidential Materials omitted and filed separately with the

Securities and Exchange Commission. A total of 7 pages were omitted. [**]

**Exhibit C**

**Development Plan**

**Exhibit D**

**Personnel Rates**

| Employee | Hourly Rate |
|---|---|
| [**] | [**] |
| [**] | [**] |
| [**] | [**] |
| [**] | [**] |
| [**] | [**] |
| [**] | [**] |
| [**] | [**] |
| [**] | [**] |

On January 1, 2019 and on January 1 of each subsequent calendar year, the foregoing rates shall be increased for the calendar year then commencing by the percentage increase, if any, in the Consumer Price Index (CPI) as of December 31 of the then most recently completed calendar year with respect to the level of the CPI on December 31, 2017. As used in this Exhibit D, CPI means the Consumer Price Index – Urban Wage Earners and Clerical Workers, US City Average, All Items, 1982-84 = 100, published by the United States Department of Labor, Bureau of Labor Statistics (or its successor equivalent index).

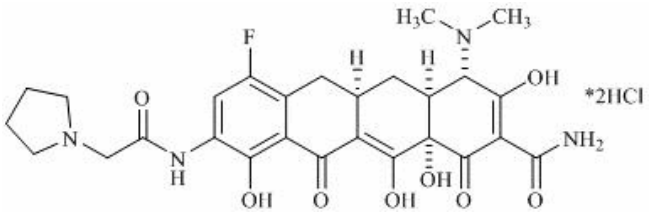
**Exhibit E**

**List of In-License Agreements Existing as of the Effective Date**

1. The Harvard Agreement

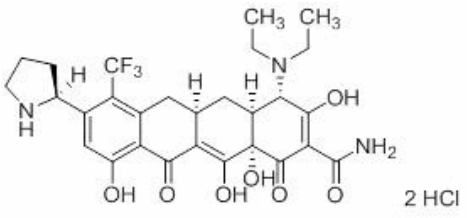
**Schedule 1.45**

**Eravacycline**



**Schedule 1.77**

**TP-6076**



**Schedule 2.04**

**Specified Tetraphase Know-How**

[**]

**Exhibit 10.31**

Tetraphase Pharmaceuticals, Inc.
480 Arsenal Street, Suite 110
Watertown, MA 02472

February 28, 2018

Larry Edwards
[address]
[address]

Dear Larry:

On behalf of Tetraphase Pharmaceuticals, Inc. (the "Company"), I am very pleased to present you with this amended and restated offer letter in connection with our offer to promote you to the position of Chief Operating Officer. The purpose of this letter is to summarize the terms of your continued employment with the Company in this new appointment, should you accept our offer.

1. **Employment**. Effective March 1, 2018 (the "Effective Date"), you will be employed to serve on a full-time basis in the position of Chief Operating Officer, reporting directly to me as President and Chief Executive Officer, Tetraphase Pharmaceuticals, Inc. As Chief Operating Officer, you will have such duties and responsibilities as are customary for such position and such other duties and responsibilities as may be assigned to you by the Company. You agree to continue to devote your full business time, best efforts, skill, knowledge, attention, and energies to the advancement of the Company's business and interests and to the performance of your duties and responsibilities as an employee of the Company.

2. **Base Compensation**. As of the Effective Date, your base salary will be increased to the rate of $15,384.62 per bi-weekly pay period (equivalent to an annualized rate of $400,000), less all applicable federal, state, and local taxes and withholdings, such base salary to be paid in installments in accordance with the Company's standard payroll practices. Such base salary may be adjusted from time to time in accordance with normal business practices and in the sole discretion of the Company.

3. **Bonus**. If the Board of Directors approves an annual bonus for fiscal year 2018 or any fiscal year thereafter, you may be eligible for a discretionary retention and performance bonus award of up to 40% of your annualized base salary in such year (the "Target Bonus"). The bonus award, if any, will be based on both individual and corporate performance and will be determined by the Board of Directors of the Company in its sole discretion. In any event, in order to be eligible for and to earn a bonus, if any, you must be an active employee of the Company on the date such bonus is distributed, as it also serves as an incentive to remain employed by the Company. Any bonus that the Board determines to be payable for a fiscal year will be paid before March 15th of the next fiscal year.

4. **Benefits**. You will continue to participate in any and all benefit programs that the Company establishes and makes available to its employees from time to time, provided that you are eligible under (and subject to all provisions of) the plan documents governing those programs. Such benefits may include: participation in group medical and dental insurance programs, term life

insurance, long-term disability insurance and participation in the Company's 401(k) plan. The benefits made available by the Company, and the rules, terms, and conditions for participation in such benefit programs, may be changed by the Company at any time and from time to time without advance notice (other than as required by such programs or under law). With respect to vacation time, you will begin to accrue vacation at 1.67 days/month or the equivalent of a maximum of 4 weeks per calendar year. Vacation may be taken at such times as may be approved by the Company. Your accrual and use of vacation time will also be subject to any and all vacation policies and procedures that the Company establishes from time to time.

5. **Stock Incentive Program.** You will continue to be eligible to participate in the Company's stock incentive program.

6. **At-Will Employment**. This letter shall not be construed as an agreement, either express or implied, to continue to employ you for any stated term, and shall in no way alter the Company's policy of employment at will, under which both you and the Company remain free to terminate the employment relationship at any time, for any reason, with or without cause, and with or without notice. Although your job duties, title, compensation and benefits, as well as the Company's personnel policies and procedures, may change from time to time, the "at-will" nature of your employment may only be changed by a written agreement signed by you and the principal executive officer of the Company, which expressly states the intention to modify the at-will nature of your employment. Similarly, nothing in this letter shall be construed as an agreement, either express or implied, to pay you any compensation or grant you any benefit beyond the end of your employment with the Company, except to the extent explicitly set forth in Section 7 hereof.

7. **Severance Benefits.** Notwithstanding your status as an at-will employee, in the event that the Company (or, as may be applicable, an acquiring or succeeding company) terminates your employment without "Cause," or you terminate your employment with the Company (or, as may be applicable, an acquiring or succeeding company) for "Good Reason" (each term as defined in Exhibit A and in either case a "Qualifying Termination"), you will be eligible for the benefits outlined in either sub-section A or subsection B (the "Severance Benefits"), subject to the terms set forth in this letter agreement:

(A)If a Qualifying Termination occurs prior to or more than twelve months following a Change in Control Event (as defined in Exhibit A), the Company will provide to you as severance pay an amount equal to twelve (12) months of your then-current base salary (subject to all applicable federal, state and local taxes and withholdings and payable over a twelve -month period in accordance with the Company's regular payroll practices). In addition, should you timely elect and be eligible to continue receiving group medical coverage pursuant to applicable "COBRA" law, and so long as the Company can provide such benefit without violating the nondiscrimination requirements of applicable law, the Company will, until the earlier of (x) the date that is twelve (12) months following your termination date and (y) the date you (or, as applicable, your beneficiaries) become eligible for coverage through a new employer, continue to pay the share of the premium for such coverage that is paid by the Company for active and similarly-situated employees who receive the same type of coverage (provided that the Company will not pay more each month than the monthly amount it was paying for your coverage when your employment ended). The remaining balance of any premium costs shall timely be paid by

you on a monthly basis (or such other basis as is required by the Company) for as long as, and to the extent that, you remain eligible for COBRA continuation.

(B) If a Qualifying Termination occurs upon or during the twelve month period commencing upon a Change in Control Event, the Company will provide to you as severance pay an amount equal to the sum of (i) twelve (12) months of your then-current base salary (subject to all applicable federal, state and local taxes and withholdings and payable over a twelve -month period in accordance with the Company's regular payroll practices) and (ii) an amount equal to 100% of your then-current annual Target Bonus (subject to all applicable federal, state and local taxes and withholdings and payable in a lump sum). In addition, should you timely elect and be eligible to continue receiving group medical coverage pursuant to applicable "COBRA" law, and so long as the Company can provide such benefit without violating the nondiscrimination requirements of applicable law, the Company will, until the earlier of (x) the date that is twelve (12) months following your termination date and (y) the date you (or, as applicable, your beneficiaries) become eligible for coverage through a new employer, continue to pay the share of the premium for such coverage that is paid by the Company for active and similarly-situated employees who receive the same type of coverage (provided that the Company will not pay more each month than the monthly amount it was paying for your coverage when your employment ended). The remaining balance of any premium costs shall timely be paid by you on a monthly basis (or such other basis as is required by the Company) for as long as, and to the extent that, you remain eligible for COBRA continuation. Further, the vesting of all stock options held by you on the date of termination shall be accelerated, such that such stock options shall become 100% fully vested and exercisable.

Your receipt of severance pay and benefits as set forth in this Section 7 is conditioned upon your full compliance with the Non-Solicitation Agreement (as defined in Section 8 below), your timely execution of a separation and release of claims agreement prepared by and satisfactory to the Company (which will include, at a minimum, a release by you of all releasable claims, non-disparagement and cooperation obligations, and reaffirmation of your continuing obligations under the Non-Solicitation Agreement) (the "Release"), and any applicable revocation period with respect to the Release expiring without revocation within 60 days (or such shorter period as may be directed by the Company) following your termination date. If the Release has been executed and any applicable revocation period has expired prior to the 60th day following your termination, then the severance payments and benefits shall commence (or in the case of any lump sum payment, be paid) on the first regular pay date after any applicable revocation period has expired (but no earlier than the 30th day following your termination date); provided, however, that if the 60th day following your termination occurs in the calendar year following the calendar year during which your termination occurs, then the severance payments shall commence (or in the case of any lump sum payment, be paid) no earlier than January 1 of such subsequent calendar year. The provision of severance pay and benefits hereunder shall be subject to the terms and conditions set forth in Section 11 hereto. In the event you breach your obligations under the Release or the Non-Solicitation Agreement, you will have no right to receive, and the Company shall not provide to you, any severance pay or benefits following the date of such breach. Such cessation of payments and benefits shall be in addition to, and not in lieu of, any and all other remedies, whether at law or in equity, available to the Company for such breach.

8. **Non-Solicitation, Non-Disclosure and Developments Agreement.** As a condition of your continued employment and promotion, you reaffirm your obligations under the Non-Solicitation, Non-Disclosure and Developments Agreement (the "Non-Solicitation Agreement") which you previously signed in connection with your employment, a copy of which is enclosed with this letter.

9. **Company Policies and Procedures**. As an employee of the Company, you remain required to comply with all Company policies and procedures. Violations of the Company's policies may lead to immediate termination of your employment. Further, the Company's premises, including all workspaces, furniture, documents, and other tangible materials, and all information technology resources of the Company (including computers, data and other electronic files, and all internet and email) remain subject to oversight and inspection by the Company at any time. Company employees should have no expectation of privacy with regard to any Company premises, materials, resources, or information.

10. **Other Agreements and Governing Law**. You represent that you are not bound by any employment contract, restrictive covenant or other restriction preventing you from continuing employment with or carrying out your responsibilities for the Company hereunder, or which is in any way inconsistent with the terms of this letter. Please note that this amended and restated offer letter is your formal offer of continued employment and supersedes any and all prior or contemporaneous agreements, discussions and understandings, whether written or oral, relating to the subject matter of this letter or your employment with the Company, including without limitation the previous offer letter between you and the Company dated May 21, 2015. The resolution of any disputes under this letter will be governed by Massachusetts law.

11. **Section 409A of the Code.**

Subject to the provisions in this Section 11, any severance payments or benefits under this letter will begin only upon the date of your "separation from service" (determined as set forth below) which occurs on or after the date of termination of your employment. The following rules shall apply with respect to distribution of the payments and benefits, if any, to be provided to you under this letter.

(a) It is intended that each installment of the severance payments and benefits provided under this letter shall be treated as a separate "payment" for purposes of Section 409A of the Internal Revenue Code and the guidance issued thereunder ("Section 409A"). Neither you nor the Company will have the right to accelerate or defer the delivery of any such payments or benefits except to the extent specifically permitted or required by Section 409A.

(b) The determination of whether and when your separation from service from the Company has occurred shall be made and in a manner consistent with and based on the presumptions set forth in, Treasury Regulation Section 1.409A-1(h). Solely for purposes of this paragraph, "Company" shall include all persons with whom the Company would be considered a single employer under Section 414(b) and 414(c) of the Internal Revenue Code.

(c) If, as of the date of your separation from service from the Company, you are not a "specified employee" (within the meaning of Section 409A), then each installment of the severance payments and benefits provided under this letter shall be made on the dates and terms set forth in this letter.

(d) If, as of the date of your separation from service from the Company, you are a "specified employee" (within the meaning of Section 409A), then:

(i) Each installment of the severance payments and benefits due under this letter that, in accordance with the dates and terms set forth herein, will in all circumstances, regardless of when your separation from service occurs, be paid within the short-term deferral period (as defined under Section 409A) shall be treated as a short-term deferral within the meaning of Treasury Regulation Section 1.409A-1(b)(4) to the maximum extent permissible under Section 409A and shall be paid on the dates and terms set forth in this letter; and

(ii) Each installment of the severance payments and benefits due under this letter that is not described in Section 11(d)(i) and that would, absent this subsection, be paid within the six-month period following your separation from service from the Company shall not be paid until the date that is six months and one day after such separation from service (or, if earlier, your death), with any such installments that are required to be delayed being accumulated during the six-month period and paid in a lump sum on the date that is six months and one day following your separation from service and any subsequent installments, if any, being paid in accordance with the dates and terms set forth herein; provided, however, that the preceding provisions of this sentence shall not apply to any installment of payments or benefits if and to the maximum extent that that such installment is deemed to be paid under a separation pay plan that does not provide for a deferral of compensation by reason of the application of Treasury Regulation 1.409A-1(b)(9)(iii) (relating to separation pay upon an involuntary separation from service). Any installments that qualify for the exception under Treasury Regulation Section 1.409A-1(b)(9)(iii) must be paid no later than the last day of your second taxable year following the taxable year in which the separation from service occurs.

(e) All reimbursements and in-kind benefits provided under this letter shall be made or provided in accordance with the requirements of Section 409A to the extent that such reimbursements or in-kind benefits are subject to Section 409A, including, where applicable, the requirements that (i) any reimbursement is for expenses incurred during your lifetime (or during a shorter period of time specified in your offer letter), (ii) the amount of expenses eligible for reimbursement during a calendar year may not affect the expenses eligible for reimbursement in any other calendar year, (iii) the reimbursement of an eligible expense will be made on or before the last day of the calendar year following the year in which the expense is incurred and (iv) the right to reimbursement is not subject to set off or liquidation or exchange for any other benefit.

(f) Notwithstanding anything herein to the contrary, the Company makes no representation or warranty and shall have no liability to you or to any other person if the payments and benefits provided in this letter are determined to constitute deferred compensation subject to Section 409A but that do not satisfy an exemption from, or the conditions of, that section.

If you agree with the terms of your continued employment in connection with your appointment to the position of Chief Operating Officer, as set forth herein, please sign the enclosed duplicate of this letter in the space provided below and return it to me. This offer is effective through March 1, 2018. If you do not accept this offer by such date, it will be deemed revoked.

On behalf of Tetraphase Pharmaceuticals, Inc.

Guy Macdonald
President and Chief Executive Officer

The foregoing correctly sets forth the terms of my continued at-will employment by the Company. I am not relying on any representations pertaining to my employment other than those set forth above.

/s/ Larry Edwards Date: March 1, 2018
Larry Edwards

**EXHIBIT A**

Definitions

For the purposes of this amended and restated offer letter:

(1) **"Cause"** shall mean: (a) a good faith finding by the Board of Directors of the Company in its sole discretion that you have (i) failed or refused to substantially perform your assigned duties for the Company, or failed or refused to comply in any material respect with the Company's material policies or procedures, which failure or violation is not cured (provided that the Company deems that such failure or violation is curable) within 20 days following written notice from the Company to you specifying the duties not performed or the nature of the violation, (ii) engaged in dishonesty, gross negligence or misconduct, or (iii) breached any employment agreement, confidentiality agreement, non-solicitation agreement, or other agreement entered into between you and the Company; or (b) your conviction of, or the entry of a pleading of guilty or *nolo contendere* by you to, any crime involving dishonesty or moral turpitude or any felony.

(2) **"Change in Control Event"** shall mean

(a) the acquisition by an individual, entity or group (within the meaning of Section 13(d)(3) or 14(d)(2) of the Securities Exchange Act of 1934, as amended (the "Exchange Act")) (a "Person") of beneficial ownership of any capital stock of the Company if, after such acquisition, such Person beneficially owns (within the meaning of Rule 13d-3 promulgated under the Exchange Act) 50% or more of the combined voting power of the then-outstanding securities of the Company entitled to vote generally in the election of directors (the "Outstanding Company Voting Securities"); provided, however, that for purposes of this subsection (a), the following acquisitions shall not constitute a Change in Control Event: (i) any acquisition directly from the Company (excluding an acquisition pursuant to the exercise, conversion or exchange of any security exercisable for, convertible into or exchangeable for common stock or voting securities of the Company, unless the Person exercising, converting or exchanging such security acquired such security directly from the Company or an underwriter or agent of the Company), or (ii) any acquisition by any employee benefit plan (or related trust) sponsored or maintained by the Company or any corporation controlled by the Company; or

(b) the consummation of a merger, consolidation, reorganization, recapitalization or statutory share exchange involving the Company or a sale or other disposition of all or substantially all of the assets of the Company (a "Business Combination"), unless, immediately following such Business Combination all or substantially all of the individuals and entities who were the beneficial owners of the Outstanding Company Voting Securities immediately prior to such Business Combination beneficially own, directly or indirectly, more than 50% of the combined voting power of the then-outstanding securities entitled to vote generally in the election of directors, respectively, of the resulting or acquiring corporation in such Business Combination (which shall include, without limitation, a corporation which as a result of such transaction owns the Company or substantially all of the Company's assets either directly or through one or more subsidiaries) in substantially the same proportions as their ownership of the Outstanding Company Voting Securities immediately prior to such Business Combination:

provided that, where required to avoid additional taxation under Section 409A, the event that occurs must also be a "change in the ownership or effective control of a corporation, or a change in the

ownership of a substantial portion of the assets of a corporation" as defined in Treasury Regulation Section 1.409A-3(i)(5).

(3) **"Good Reason"** shall occur if a Cause event has not occurred or has not been cured, to the extent curable, and if (x) you provide written notice to the Company of the event or change you consider to constitute "Good Reason" within 30 calendar days following its occurrence, (y) you provide the Company with a period of at least 30 calendar days to cure the event or change, and (z) the "Good Reason" persists following the cure period, and you actually resign within 60 calendar days following the event or change. An event or change constituting "Good Reason" shall be limited to any of the following that occur without your prior written consent: (a) a material diminution of your duties, authority or responsibilities, provided, however, that the assignment of different duties to you by the Company involving a reasonably comparable level of responsibility shall not, by itself, constitute "Good Reason," and provided, further, that a change in your duties, authority or responsibilities solely as a result of the Company's acquisition by or merger with another entity, if you continue to have a comparatively senior role relative to the Company or its successor following such event, shall not, by itself, constitute "Good Reason"; (b) a material diminution in your base compensation, or (c) the relocation of the principal place at which you provide services to the Company by at least 50 miles and to a location such that your daily commuting distance is increased.

**Exhibit 21.1**

**SUBSIDIARIES OF THE REGISTRANT**

| Name | Jurisdiction of Organization | Percentage Ownership |
|---|---|---|
| Tetraphase Pharma Securities, Inc. | Massachusetts | 100% |
| Tetraphase Pharmaceuticals (Bermuda) Ltd. | Bermuda | 100% |
| Tetraphase Ireland Limited | Republic of Ireland | * |
| Tetraphase UK Limited | United Kingdom | * |

*100% owned by Tetraphase Pharmaceuticals (Bermuda) Ltd.

**Exhibit 23.1**

**Consent of Independent Registered Public Accounting Firm**

We consent to the incorporation by reference in the following Registration Statements:

(1) Registration Statement (Form S-8 No. 333-209991) pertaining to the 2013 Stock Incentive Plan and Inducement Stock Option Awards of Tetraphase Pharmaceuticals, Inc.,

(2) Registration Statement (Form S-8 No. 333-198098) pertaining to the 2014 Employee Stock Purchase Plan of Tetraphase Pharmaceuticals, Inc.,

(3) Registration Statement (Form S-8 No. 333-194125, No. 333-202576 and No. 333-216742) pertaining to the 2013 Stock Incentive Plan of Tetraphase Pharmaceuticals, Inc.,

(4) Registration Statement (Form S-8 No. 333-189361) pertaining to the 2006 Stock Incentive Plan and the 2013 Stock Incentive Plan of Tetraphase Pharmaceuticals, Inc., and

(5) Registration Statement (Form S-3 No. 333-214500 and No. 333-222699) of Tetraphase Pharmaceuticals, Inc.

of our reports dated March 6, 2018, with respect to the consolidated financial statements of Tetraphase Pharmaceuticals, Inc. and the effectiveness of internal control over financial reporting of Tetraphase Pharmaceuticals, Inc. included in this Annual Report (Form 10-K) of Tetraphase Pharmaceuticals, Inc. for the year ended December 31, 2017.

/s/ Ernst & Young LLP

Boston, Massachusetts
March 6, 2018

**Exhibit 31.1**

**CERTIFICATION**

I, Guy Macdonald, certify that:

1. I have reviewed this Annual Report on Form 10-K of Tetraphase Pharmaceuticals, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b. Designed such internal control over financial reporting or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 6, 2018

/s/ Guy Macdonald
Guy Macdonald
Chief Executive Officer

**Exhibit 31.2**

**CERTIFICATION**

I, Kamalam Unninayar, certify that:

1. I have reviewed this Annual Report on Form 10-K of Tetraphase Pharmaceuticals, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b. Designed such internal control over financial reporting or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 6, 2018

/s/ Kamalam Unninayar
Kamalam Unninayar
Chief Financial Officer

**EXHIBIT 32.1**

**CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,**
**AS ADOPTED PURSUANT TO**
**SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with the Annual Report on Form 10-K of Tetraphase Pharmaceuticals, Inc. (the "Company") for the fiscal year ended December 31, 2017 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Guy Macdonald, Chief Executive Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, that, to his knowledge on the date hereof:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 6, 2018

/s/ Guy Macdonald
Guy Macdonald
Chief Executive Officer

**EXHIBIT 32.2**

**CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,**
**AS ADOPTED PURSUANT TO**
**SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with the Annual Report on Form 10-K of Tetraphase Pharmaceuticals, Inc. (the "Company") for the fiscal year ended December 31, 2017 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Kamalam Unninayar, Chief Financial Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, that, to her knowledge on the date hereof:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 6, 2018

/s/ Kamalam Unninayar
Kamalam Unninayar
Chief Financial Officer